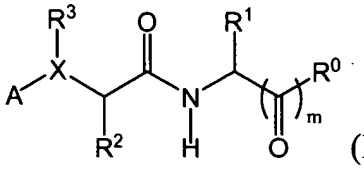
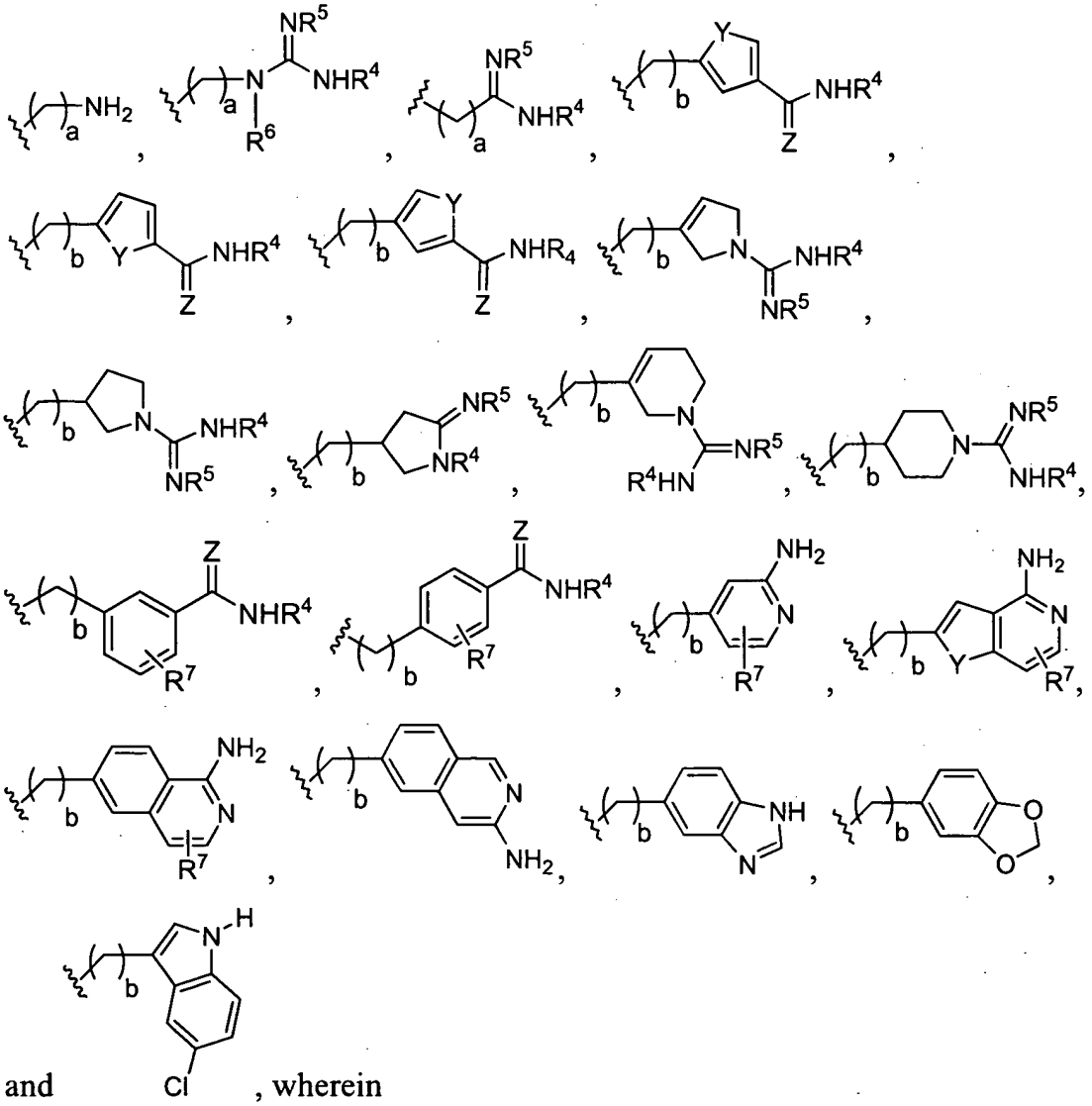
CLAIMS

1. A compound of formula I:



(I), or a pharmaceutically acceptable salt or prodrug thereof, wherein

R^1 is selected from the group consisting of:



and , wherein

R^4 is H or C_{1-6} alkyl, R^5 is H, C_{1-6} alkyl, OH, NH_2, NO_2, CO_2R^{5a}, wherein R^{5a} is C_{1-6} alkyl, or R^5 taken together with R^4 forms a 5- or 6-membered ring, R^6 is

H, OH, C_{1-6} alkyl, or when taken together with R^4, forms a 5- or 6-membered ring, R^7 is H, OH, SH, NH_2, NO_2, optionally substituted C_{1-6} alkyl, halogen, or CF_3, Y is O, S, or NR^4, and Z is NR^5 or (H,H);

R^2 is H or an optionally substituted C_{1-6} alkyl, C_{2-6} alkenyl, C_{3-8} cycloalkyl, C_{7-16} aralkyl, C_{8-16} aralkenyl, C_6 or C_{10} aryl, C_{2-9} heterocyclyl, C_{2-15} heteroaralkyl, or C_{3-15} heteroaralkenyl, or when taken together with X and R^3 forms an optionally substituted C_6 aryl group or an optionally substituted C_3-C_5 heteroaryl group; a is an integer from 0-5; b is an integer from 0-2;

X is C or N;

R^3 is H or optionally substituted C_{1-6} alkyl, or together with X and A forms an optionally substituted C_{2-5} heterocylic ring, or together with X and R^2 forms an optionally substituted C_6 aryl group or an optionally substituted C_3-C_5 heteroaryl group;

A is R^8-AA_2, where AA_2 is a covalent bond or a peptide chain of one to five natural or unnatural alpha-amino acid residues of D- or L- configuration, wherein R^8 is H, C_{2-7} acyl, C_{7-11} aroyl, C_{3-10} heteroaroyl, C_{2-7} alkoxycarbonyl, C_{4-9} cycloalkoxycarbonyl, C_{8-17} aralkoxycarbonyl, C_7 or C_{11} aryloxycarbonyl, aminocarbonyl, C_{2-7} alkylaminocarbonyl, C_{3-13} dialkylaminocarbonyl, C_{4-9} cycloalkylaminocarbonyl, C_{8-17} aralkylaminocarbonyl, C_7 or C_{11} arylaminocarbonyl, C_{3-10} heterocyclylaminocarbonyl, C_{3-16} heteroaralkylaminocarbonyl, C_{2-7} alkylthiocarbonyl, C_{7-11} arylthiocarbonyl, C_{3-10} heteroarylthiocarbonyl, C_{2-7} alkoxythiocarbonyl, C_{4-9} cycloalkoxythiocarbonyl, C_{8-17} aralkoxythiocarbonyl, C_7 or C_{11} aryloxythiocarbonyl, aminothiocarbonyl, C_{2-7} alkylaminothiocarbonyl, C_{3-13} dialkylaminothiocarbonyl, C_{4-9} cycloalkylaminothiocarbonyl, C_{8-17} aralkylaminothiocarbonyl, C_7 or C_{11} arylaminothiocarbonyl, C_{3-10} heterocyclylaminothiocarbonyl, C_{3-16} heteroaralkylaminothiocarbonyl, C_{1-6} alkylsulfonyl, C_{3-8} cycloalkylsulfonyl, C_{7-16} aralkylsulfonyl, C_6 or C_{10} arylsulfonyl, C_{2-9} heterocyclylsulfonyl, or C_{2-15} heteroaralkylsulfonyl,

or A together with X and R^3 forms an optionally substituted C_{2-5} heterocylic ring; and

m is 0 or 1, wherein

when m is 1, R^0 is an optionally substituted C_{1-6} alkyl, C_{2-6} alkenyl, C_{3-8} cycloalkyl, C_{7-16} aralkyl, C_{8-16} aralkenyl, C_6 or C_{10} aryl, C_{1-9} heterocyclyl, C_{2-15} heteroaralkyl, C_{3-15} heteroaralkenyl, or $C(O)R^9$, wherein R^9 is an optionally substituted C_{1-6} alkyl, C_{2-6} alkenyl, C_{1-8} cycloalkyl, C_{7-16} aralkyl, C_{8-16} aralkenyl, C_6 or C_{10} aryl, C_{1-9} heterocyclyl, C_{2-15} heteroaralkyl, C_{3-15} heteroaralkenyl, C_{1-6} alkyloxy, C_6 or C_{10} aryloxy, C_{1-9} heteroaryloxy, C_{7-16} aralkyloxy, C_{1-6} alkylthio, C_{3-8} cycloalkylthio, C_6 or C_{10} arylthio, C_{7-16} aralkylthio, C_{1-6} alkylamino, C_{2-12} dialkylamino, C_{3-8} cycloalkylamino, C_{7-16} aralkylamino, C_6 or C_{10} arylamino, C_{2-9} heterocyclylamino, or C_{2-15} heteroaralkylamino, with the proviso that the amino acid of AA_2 that is covalently linked to X is not D-phenylalanine when R^8 is C_{1-6} alkylsufonyl or C_{7-16} aralkylsulfonyl;

when m is 0, R^0 is H, CHO, CN, or $B(OR^9)_2$, wherein R^9 is H, C_{1-6} alkyl, or taken together forms a C_{2-4} cyclic boronate ester, or R^0 is an optionally substituted C_{1-6} alkyl, C_{2-6} alkenyl, C_{3-8} cycloalkyl, C_{7-16} aralkyl, C_{8-16} aralkenyl, C_6 or C_{10} aryl, C_{1-9} heterocyclyl, C_{2-15} heteroaralkyl, or C_{3-15} heteroaralkenyl, with the proviso that the amino acid of AA_2 that is covalently linked to X is not D-cyclohexylglycine when R^8 is C_{1-6} alkylsulfonyl or C_{7-16} aralkylsulfonyl.

2. The compound of claim 1, wherein R^0 is 2-thiazole, 2-(4-methylthiazole), 2-(5-methylthiazole), 2-(4,5-dimethylthiazole), 2-(5-(2-hydroxyethyl)thiazole), or 2-N-methylimidazole.

3. The compound of claim 1, wherein

R^2 is H or a substituted C_{1-6} alkyl, C_{2-6} alkenyl, C_{3-8} cycloalkyl, C_{7-16} aralkyl, C_{8-16} aralkenyl, C_6 or C_{10} aryl, C_{1-9} heterocyclyl, C_{2-15} heteroaralkyl, or C_{3-15} heteroaralkenyl;

X is N;

a is an integer from 1-4;

b is an integer from 0-2;

AA_2 is a covalent bond and R^8 is B-Y^1-$(CH_2)_n$-K-C(O)-, wherein n is an integer from 0-6, K together with -C(O)-, X, and R^3 forms an optionally substituted C_{2-5} heterocyclyl group or K is a single bond, NR^9, O, S, C(O), $CH(OR^{10})$, or -$CH(NHR^{11})$, wherein R^9 is H, OH, or C_{1-6} alkyl, each of R^{10} R^{11} is, independently, H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{3-8} cycloalkyl, C_{7-16} aralkyl, C_{8-16} aralkenyl, C_6 or C_{10} aryl, C_{1-9} heterocyclyl, C_{2-15} heteroaralkyl, C_{3-15} heteroaralkenyl, C_{2-7} acyl, C_{7-11} aroyl, C_{3-10} heteroaroyl, C_{2-7} alkoxycarbonyl, C_{4-9} cycloalkoxycarbonyl, C_{8-17} aralkoxycarbonyl, C_7 or C_{11} aryloxycarbonyl, aminocarbonyl, C_{2-7} alkylaminocarbonyl, C_{3-13} dialkylaminocarbonyl, C_{4-9} cycloalkylaminocarbonyl, C_{8-17} aralkylaminocarbonyl, C_7 or C_{11} arylaminocarbonyl, C_{3-10} heterocyclylaminocarbonyl, C_{3-16} heteroaralkylaminocarbonyl, C_{2-7} alkylthiocarbonyl, C_{7-11} arylthiocarbonyl, C_{3-10} heteroarylthiocarbonyl, C_{2-7} alkoxythiocarbonyl, C_{4-9} cycloalkoxythiocarbonyl, C_{8-17} aralkoxythiocarbonyl, C_7 or C_{11} aryloxythiocarbonyl, aminothiocarbonyl, C_{2-7} alkylaminothiocarbonyl, C_{3-13} dialkylaminothiocarbonyl, C_{4-9} cycloalkylaminothiocarbonyl, C_{8-17} aralkylaminothiocarbonyl, C_7 or C_{11} arylaminothiocarbonyl, C_{3-10} heterocyclylaminothiocarbonyl, C_{3-16} heteroaralkylaminothiocarbonyl, C_{1-6} alkylsulfonyl, C_{3-8} cycloalkylsulfonyl, C_{7-16} aralkylsulfonyl, C_6 or C_{10} arylsulfonyl, C_{2-9} heterocyclylsulfonyl, or C_{2-15} heteroaralkylsulfonyl, Y^1 is O, S, NR^{18}, or a covalent bond, wherein R^{18} is H or C_{1-6} alkyl, wherein when Y^1 is a covalent bond, B is an optionally substituted C_{1-6} alkyl, C_{2-6} alkenyl, C_{3-8} cycloalkyl, C_6 or C_{10} aryl, C_{1-9} heterocyclyl, C_{7-16} aralkyl, C_{8-16} aralkenyl, C_{2-15} heteroaralkyl, C_{3-15} heteroaralkenyl, C_{1-6} alkylsulfonyl amino, and when Y^1 is O, S, or NR^{18}, and B is an optionally substituted C_{1-6} alkyl, C_{2-6} alkenyl, C_{3-8} cycloalkyl, C_{7-16} aralkyl, C_{8-16} aralkenyl, C_6 or C_{10} aryl, C_{1-9} heterocyclyl, C_{2-15} heteroaralkyl, C_{3-15} heteroaralkenyl, C_{2-7} acyl, C_{7-11} aroyl, C_{3-10}

heteroaroyl, C_{2-7} alkoxycarbonyl, C_{4-9} cycloalkoxycarbonyl, C_{8-17} aralkoxycarbonyl, C_7 or C_{11} aryloxycarbonyl, C_{2-10} heterocyclyloxycarbonyl, aminocarbonyl, C_{2-7} alkylaminocarbonyl, C_{3-13} dialkylaminocarbonyl, C_{4-9} cycloalkylaminocarbonyl, C_{8-17} aralkylaminocarbonyl, C_7 or C_{11} arylaminocarbonyl, C_{3-10} heterocyclylaminocarbonyl, C_{3-16} heteroaralkylaminocarbonyl, C_{2-7} alkylthiocarbonyl, C_{7-11} arylthiocarbonyl, C_{3-10} heteroarylthiocarbonyl, C_{2-7} alkoxythiocarbonyl, C_{4-9} cycloalkoxythiocarbonyl, C_{8-17} aralkoxythiocarbonyl, C_7 or C_{11} aryloxythiocarbonyl, aminothiocarbonyl, C_{2-7} alkylaminothiocarbonyl, C_{3-13} dialkylaminothiocarbonyl, C_{4-9} cycloalkylaminothiocarbonyl, C_{8-17} aralkylaminothiocarbonyl, C_7 or C_{11} arylaminothiocarbonyl, C_{3-10} heterocyclylaminothiocarbonyl, C_{3-16} heteroaralkylaminothiocarbonyl;

R^3 is H or optionally substituted C_{1-6} alkyl, or together with X and A forms an optionally substituted C_{2-5} heterocylic ring;

R^0 is -E-J, wherein

when m is 0,

E is a single bond to J, wherein J is H or an optionally substituted C_{1-6} alkyl; and

when m is 1,

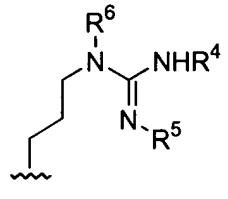
E is selected from the group consisting of a single bond to J, -C(O)O-, -C(O)S-, and -C(O)NR^{10}-, wherein R^{10} is H or C_{1-6} alkyl and J is an optionally substituted C_{1-6} alkyl, C_{2-6} alkenyl, C_{3-8} cycloalkyl, C_{7-16} aralkyl, C_{8-16} aralkenyl, C_6 or C_{10} aryl, C_{1-9} heterocyclyl, C_{2-15} heteroaralkyl, or C_{3-15} heteroaralkenyl.

4. The compound of claim 3, wherein R^8 is B-Y^1-$(CH_2)_n$-K-C(O)-, wherein K is oxo or CHOH, n is 0, and B-Y^1 is phenyl, 4-chlorophenyl, 3-chlorophenyl, 3,4-dichlorophenyl, 3,5-dichlorophenyl, 3-fluorophenyl, 4-fluorophenyl, 3,4-difluorophenyl, and 3,5-difluorophenyl.

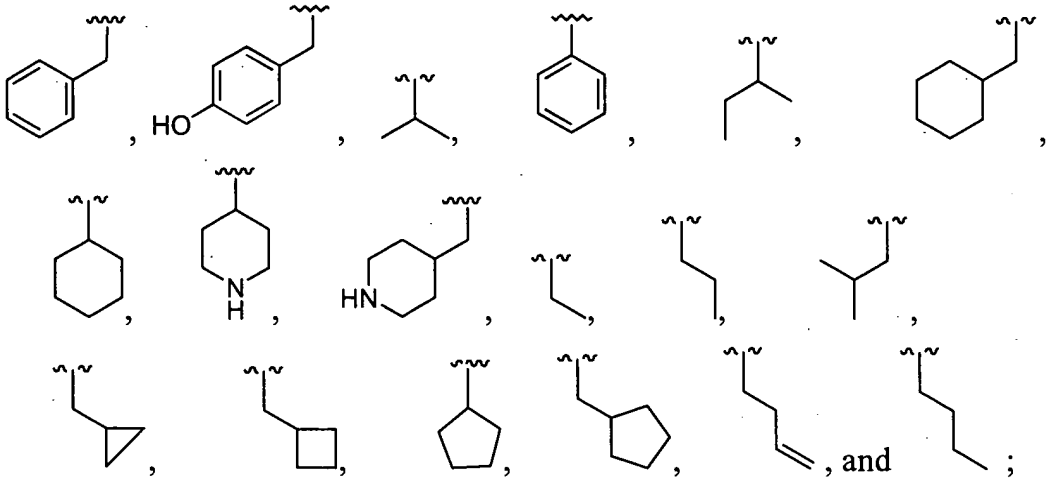
5. The compound of claim 1, wherein

m is 1;

R^0 is an optionally substituted 2-thiazole or 2-benzthiazole ring;

R^1 is  ;

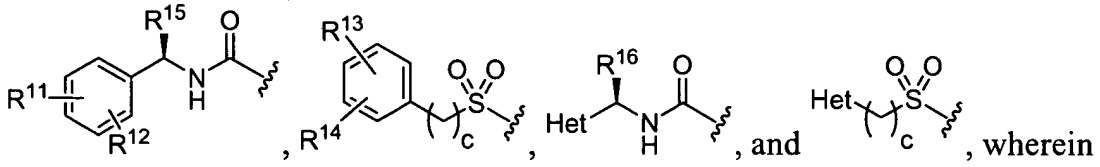
R^2 is selected from the group consisting of:



X is N; and R^3 is H.

6. The compound of claim 5, wherein

A is R^8-AA_2, wherein AA_2 is a single natural or unnatural alpha-amino acid residue and R^8 is selected from the group consisting of:



, wherein

c is 0 or 1;

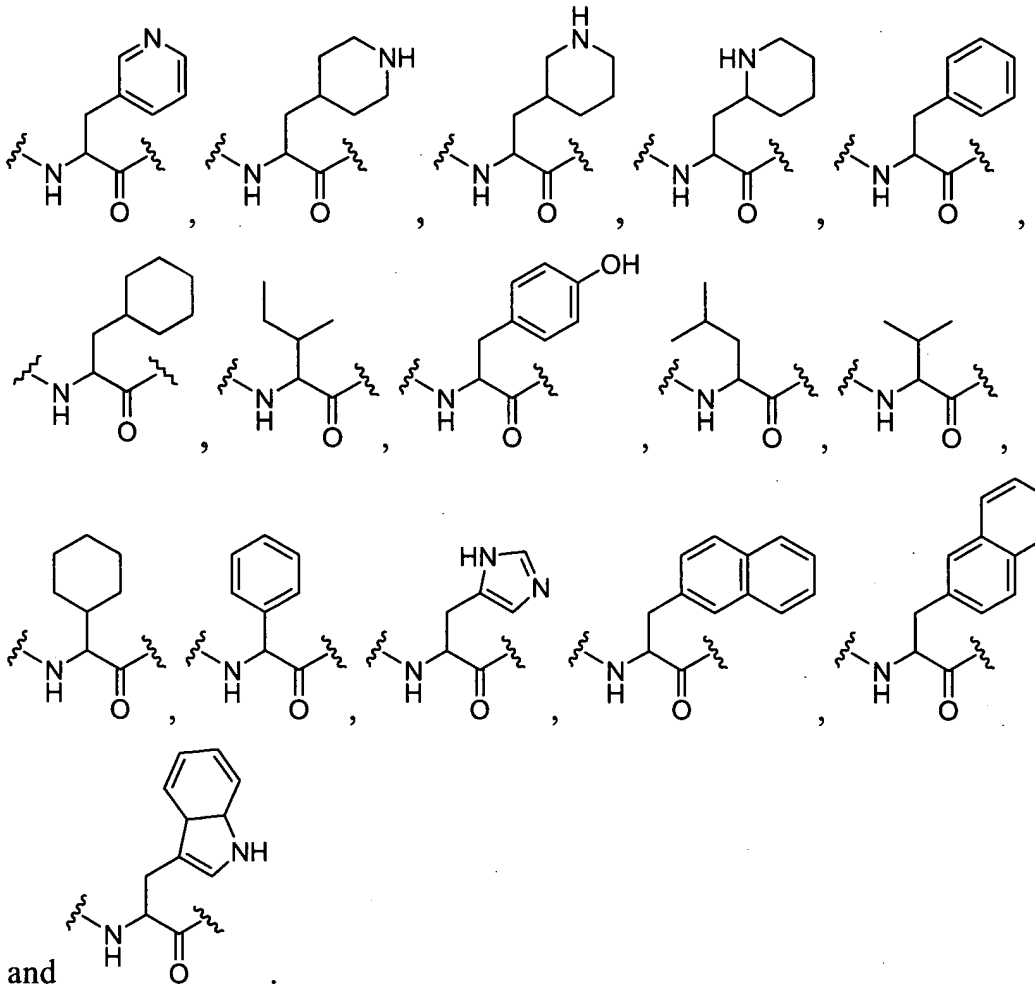
each of R^{11}, R^{12}, R^{13}, and R^{14} is, independently, C_{2-7} alkanoyl, C_{1-6} alkyl, C_{1-6} alkenyl, C_{1-6} alkoxy, C_{2-12} alkoxyalkyl, C_{1-6} alkylsulfinyl, C_{2-12} alkylsulfinylalkyl, C_{1-6} alkylsulfonyl, C_6 or C_{10} aryl, C_{7-16} arylalkyl, amino, C_{1-6} aminoalkyl, C_7 or C_{11}

aryloyl, azido, C_{1-6} azidoalkyl, carboxaldehyde, carboxamide, carboxyl, C_{2-7} (carboxaldehyde)alkyl, C_{3-8} cycloalkyl, C_{4-14} cycloalkylalkyl, halo, C_{1-6} haloalkyl, C_{1-9} heterocyclyl, C_{1-9} (heterocyclyl)oxy, C_{2-10} (heterocyclyl)oyl, hydroxy, C_{1-6} hydroxyalkyl, nitro, C_{1-6} nitroalkyl, N-protected amino, N-protected aminoalkyl, C_{1-6} thioalkoxy, C_{2-12} thioalkoxyalkyl, $-(CH_2)_qCO_2R^A$, wherein q is zero to four and R^A is selected from the group consisting of (a) C_{1-6} alkyl, (b) C_6 or C_{10} aryl and (c) C_{7-16} arylalkyl, wherein the alkylene group is of one to six carbon atoms, $-(CH_2)_qCONR^BR^C$, wherein q is zero to four and R^B and R^C are independently selected from the group consisting of (a) hydrogen, (b) C_{1-6} alkyl, (c) C_6 or C_{10} aryl and (d) C_{7-16} arylalkyl, wherein the alkylene group is of one to six carbon atoms, $-(CH_2)_qSO_2R^D$, wherein q is zero to four and R^D is selected from the group consisting of (a) hydrogen, (b) C_{1-6} alkyl, (c) C_6 or C_{10} aryl and (d) C_{7-16} arylalkyl, wherein the alkylene group is of one to six carbon atoms, $-(CH_2)_qSO_2NR^ER^F$, wherein q is zero to four and R^E and R^F are independently selected from the group consisting of (a) hydrogen, (b) C_{1-6} alkyl, (c) C_6 or C_{10} aryl and (d) C_{7-16} arylalkyl, wherein the alkylene group is of one to six carbon atoms, $-(CH_2)_qNR^GR^H$, wherein q is zero to four and R^G and R^H are independently selected from the group consisting of (a) hydrogen, (b) an N-protecting group, (c) alkyl of one to six carbon atoms, (d) alkenyl of two to six carbon atoms, (e) alkynyl of two to six carbon atoms, (f) C_6 or C_{10} aryl, (g) C_{7-16} arylalkyl, wherein the alkylene group is of one to six carbon atoms, (h) cycloalkyl of three to eight carbon atoms, and (i) cycloalkylalkyl, wherein the cycloalkyl group is of three to eight carbon atoms, and the alkylene group is of one to ten carbon atoms, with the proviso that no two groups are bound to the nitrogen atom through a carbonyl group or a sulfonyl group, C_{1-4} perfluoroalkyl, C_{1-4} perfluoroalkoxy; C_6 or C_{10} aryloxy, C_{3-8} cycloalkoxy, C_{4-14} cycloalkylalkoxy, or C_{7-16} arylalkoxy; and

each of R^{15} and R^{16} is, independently, H, C_{1-6} alkyl; C_{1-6} hydroxyalkyl; C_{1-4} perfluoroalkyl, cyano, halo, $-(CH_2)_qCO_2R^A$, $-(CH_2)_qCONR^BR^C$, $-(CH_2)_qSO_2R^D$, -

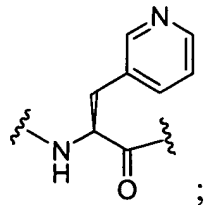
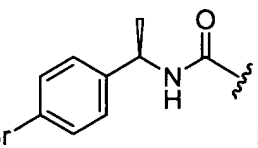
$(CH_2)_qSO_2NR^ER^F$, $-(CH_2)_qNR^GR^H$, wherein q is zero to two and R^A, R^B, R^C, R^D, R^E, R^F, R^G, and R^H are as defined above.

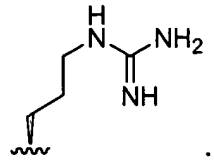
7. The compound of claim 6, wherein AA_2 is selected from the group consisting of:



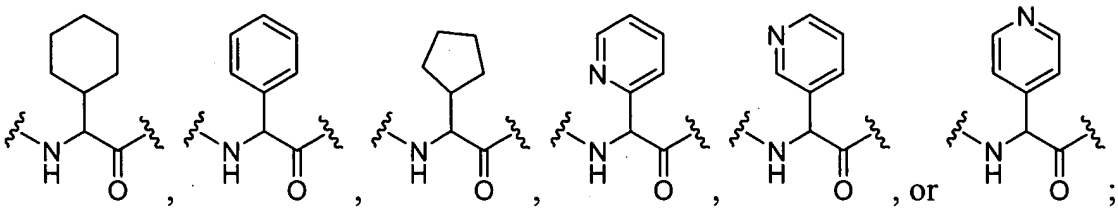
and .

8. The compound of claim 7, wherein

AA_2 is  ; R^8 is  ; R^2 is  ; and

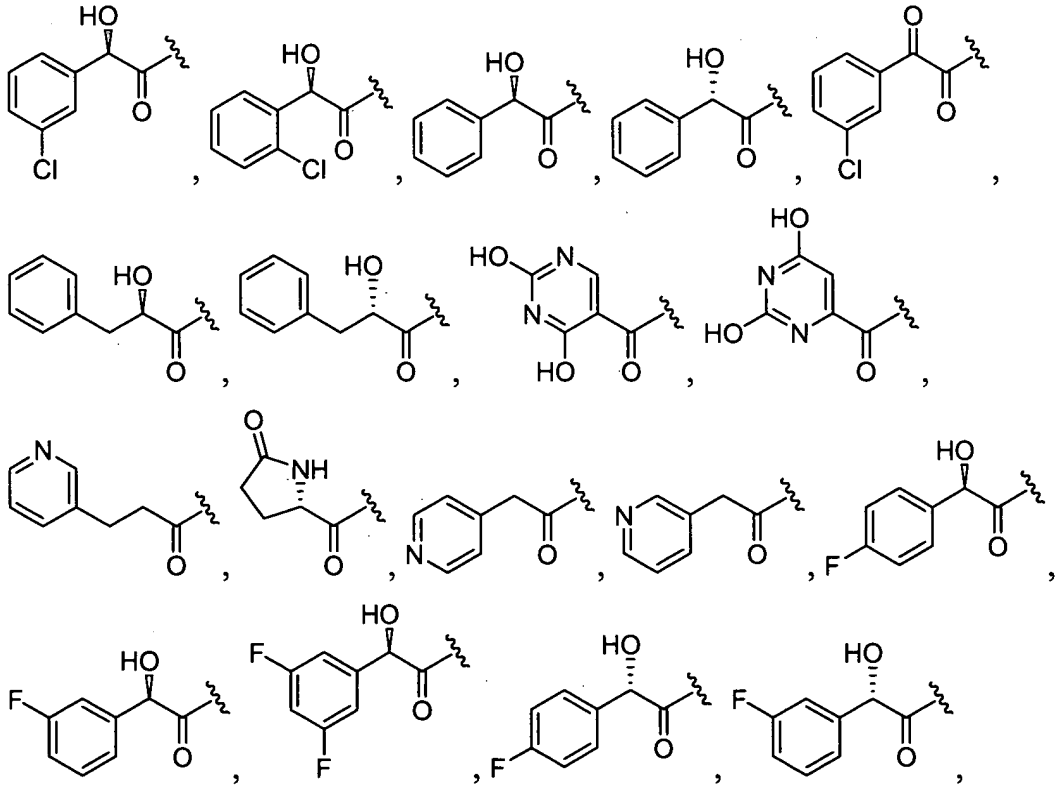
R^1 is  .

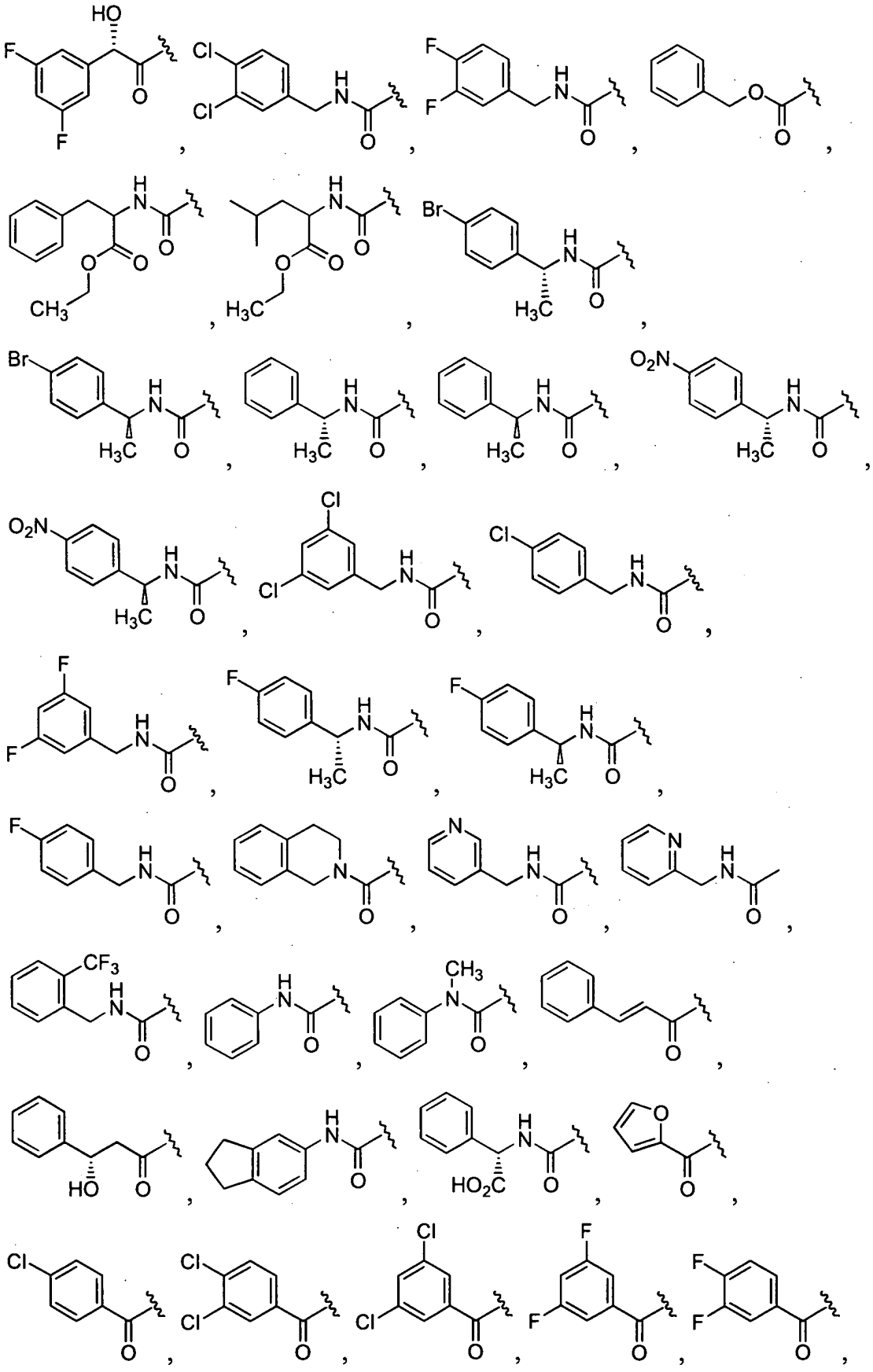
9. The compound of claim 5, wherein AA_2 is

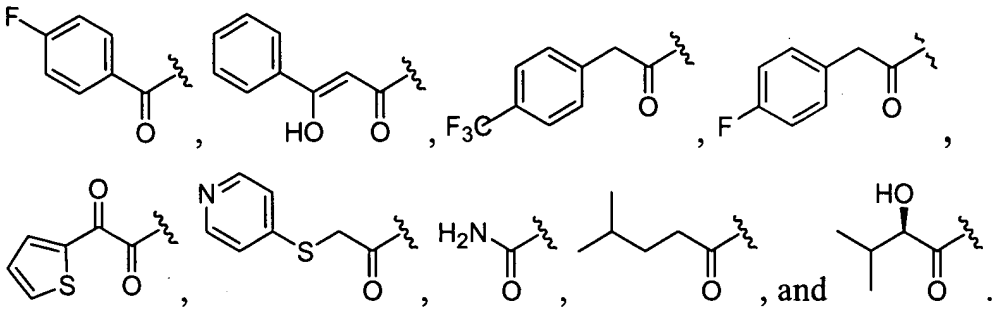


and R^8 is selected from the group consisting of: α-toluenesulfonyl, (methyl-3-benzoate)methanesulfonyl, 2-nitro-α-toluenesulfonyl, 1-propanesulfonyl, 3-carboxyl-α-toluenesulfonyl, and 3-chloropropanesulfonyl.

10. The compound of claim 5, wherein A is selected from the group consisting of:

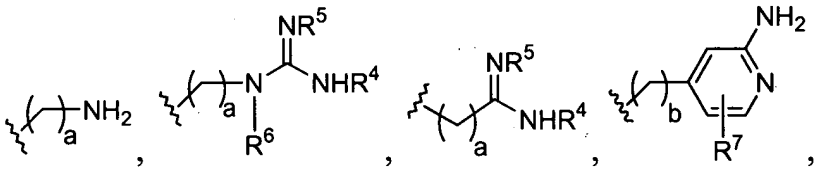


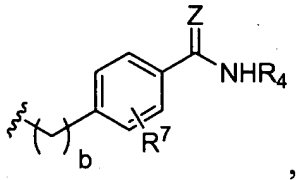




11. The compound of claim 1, wherein

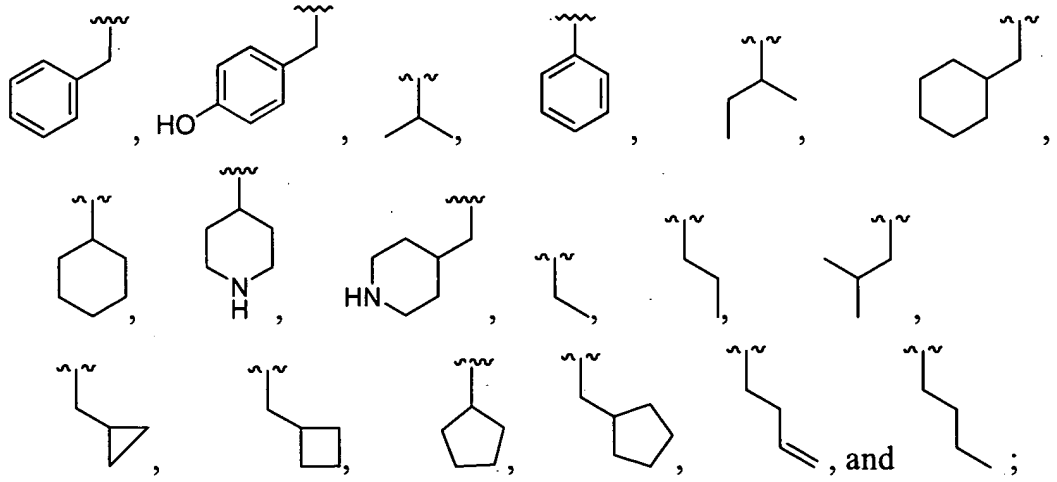
R^1 is selected from the group consisting of:





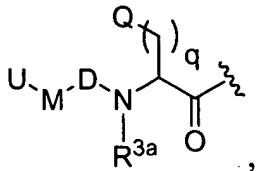
, wherein a is an integer from 1-4, b is an integer from 0-2, R^4 is H or C_{1-6} alkyl, R^5 is H, C_{1-6} alkyl, OH, NH_2, NO_2, CO_2R^{5a}, wherein R^{5a} is C_{1-6} alkyl, or R^5 taken together with R^4 forms a 5- or 6-membered ring, and R^7 is H, OH, SH, NH_2, NO_2, optionally substituted C_{1-6} alkyl, halogen, or CF_3;

R^2 is selected from the group consisting of:



X is N;

R^3 is H;

A is  , wherein

R^{3a} is H, C_{1-6} alkyl, or together with M forms a 5- or 6-membered ring,

D is C(O), C(S), or $S(O)_2$,

q is an integer from 0-4,

Q is an optionally substituted C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{1-9} heterocyclyl, C_6 or C_{10} aryl, C_{1-6} alkyloxy, C_{3-8} cycloalkyloxy, C_6 or C_{10} aryloxy, C_{2-9} heterocyclyloxy, C_{1-6} alkylthio, C_{3-8} cycloalkylthio, C_6 or C_{10} arylthio, C_{1-6} alkylamino, C_{2-12} dialkylamino, C_{7-16} aralkylamino, C_6 or C_{10} arylamino, C_{2-9} heterocyclylamino, aminocarbonyl, C_{2-7} alkylaminocarbonyl, C_{3-13} dialkylaminocarbonyl, amino, amidino, guanidino, ureido, hydroxy, or carboxy, with the proviso that when q is 1, Q is not phenyl,

M is single bond, NR^{3b}, O, or S, wherein R^{3b} is H, C_{1-6} alkyl, or when taken together with M, D, N, and R^{3a} forms a 5- or 6-membered ring, and

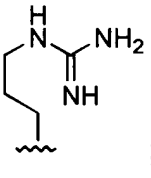
U is an optionally substituted C_{1-6} alkyl, C_{2-6} alkenyl, C_{3-8} cycloalkyl, C_{1-9} heterocyclyl, C_{7-16} aralkyl, C_{8-16} aralkenyl, C_6 or C_{10} aryl, C_{2-15} heterocyclyalkyl, or C_{3-15} heteroaralkenyl, wherein

when m is 1, R^0 is an optionally substituted C_6 or C_{10} aryl C_{1-9} heterocyclyl, or when m is 0, R^0 is H or C_{1-6} alkyl.

12. The compound of claim 11, wherein

m is 1;

R^0 is an optionally substituted 2-thiazole or 2-benzthiazole ring;

R^1 is  ;

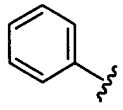
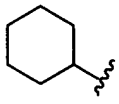
R^2 is 2-methylpropyl;

R^{3a} is H;

D is $S(O)_2$;

M is a single bond;

q is 0;

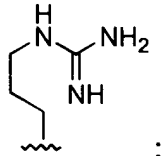
Q is  or  , and

U is selected from the group consisting of: benzyl, 3-methylcarboxybenzyl, 3-carboxybenzyl, 2-nitrobenzyl, 1-propyl, and 3-chloropropyl.

13. The compound of claim 11, wherein

m is 1;

R^0 is an optionally substituted 2-thiazole or 2-benzthiazole ring;

R^1 is  ;

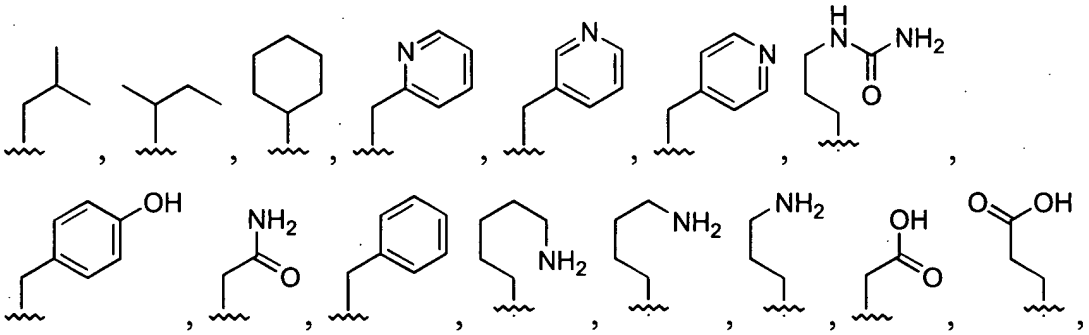
R^{3a} is H;

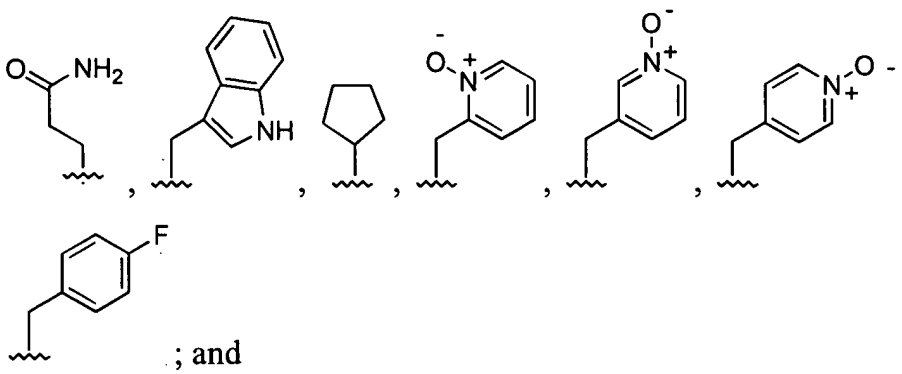
D is C(O);

M is NR^{3b}, wherein R^{3b} is H;

q is 0;

Q is selected from the group consisting of:





, and

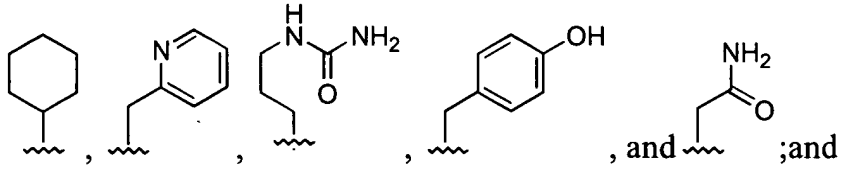
; and

U is selected from the group consisting of: 2-chlorobenzyl, 3-chlorobenzyl, 4-chlorobenzyl, 2,3-dichlorobenzyl, 2,4-dichlorobenzyl, 2,5-dichlorobenzyl, 2,6-dichlorobenzyl, 3,4-dichlorobenzyl, 3,5-dichlorobenzyl, 2-fluorobenzyl, 3-fluorobenzyl, 4-fluorobenzyl, 2,3-difluorobenzyl, 2,4-difluorobenzyl, 2,5-difluorobenzyl, 2,6-difluorobenzyl, 3,4-difluorobenzyl, 3,5-difluorobenzyl, (*R*)-α-methyl-4-bromobenzyl, (*S*)-α-methyl-4-bromobenzyl, (*R*)-α-methyl-4-chlorobenzyl, (*S*)-α-methyl-4-chlorobenzyl, (*R*)-α-methyl-4-fluorobenzyl, (*S*)-α-methyl-4-fluorobenzyl, 2-trifluoromethylbenzyl, 2-methylbenzyl, 3-methylbenzyl, 4-methylbenzyl, 2-phenylacetic acid, 2-pyridylmethyl, 3-pyridylmethyl, 4-pyridylmethyl, phenyl, and indanyl.

14. The compound of claim 13, wherein

R^2 is  ;

Q is selected from the group consisting of:



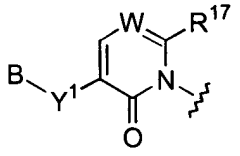
, and ;and

U is (*R*)-α-methyl-4-bromobenzyl.

15. The compound of claim 11, wherein

U is $CHR^{3c}R^{3d}$, wherein R^{3c} is an optionally substituted C_6 or C_{10} aryl or C_{1-9} heterocyclyl, and R^{3d} is H, C_{1-6} alkyl, C_{2-6} alkenyl, or together with R^{3c} forms a fused bicyclic ring.

16. The compound of claim 3, wherein AA_2 is a covalent bond and R^8 is B-Y^1-$(CH_2)_n$-K-C(O)-, wherein K-C(O)-, X, and R^3 together forms a heterocyclyl group having the formula X:



(X), wherein

W is CH or N;

R^{17} is hydrogen or an optionally substituted C_{1-6} alkyl, C_{2-6} alkenyl, C_{3-8} cycloalkyl, C_{7-16} aralkyl, C_{8-16} aralkenyl, C_6 or C_{10} aryl, C_{1-9} heterocyclyl, C_{2-15} heteroaralkyl, C_{1-6} alkylthio, C_{3-8} cycloalkylthio, C_6 or C_{10} arylthio, C_{7-16} aralkylthio, C_{2-9} heterocyclylthio, C_{2-15} heteroaralkylthio, C_{1-6} alkylamino, C_{2-12} dialkylamino C_{3-8} cycloalkylamino, C_{7-16} aralkylamino, C_6 or C_{10} arylamino, or C_{2-9} heterocyclylamino;

Y^1 is O, S, NR^{18}, or a covalent bond, wherein R^{18} is H or C_{1-6} alkyl, wherein

when Y^1 is a covalent bond, B is an optionally substituted C_{1-6} alkyl, C_{2-6} alkenyl, C_{3-8} cycloalkyl, C_6 or C_{10} aryl, C_{1-9} heterocyclyl, C_{7-16} aralkyl, C_{8-16} aralkenyl, C_{2-15} heteroaralkyl, C_{3-15} heteroaralkenyl, C_{1-6} alkylsulfonyl amino, C_{3-8} cycloalkylsulfonylamino, C_{7-16} aralkylsulfonylamino, C_6 or C_{10} arylsulfonylamino, C_{2-9} heterocyclylsulfonylamino, or C_{2-15} heteroaralkylsulfonylamino, or

when Y^1 is O, S, or NR^{18}, B is an optionally substituted C_{1-6} alkyl, C_{2-6} alkenyl, C_{3-8} cycloalkyl, C_{7-16} aralkyl, C_{8-16} aralkenyl, C_6 or C_{10} aryl, C_{1-9} heterocyclyl, C_{2-15} heteroaralkyl, C_{3-15} heteroaralkenyl, C_{2-7} acyl, C_{7-11} aroyl, C_{3-10} heteroaroyl, C_{2-7} alkoxycarbonyl, C_{4-9} cycloalkoxycarbonyl, C_{8-17} aralkoxycarbonyl, C_7 or C_{11}

aryloxycarbonyl, C_{2-10} heterocyclyloxycarbonyl, aminocarbonyl, C_{2-7} alkylaminocarbonyl, C_{3-13} dialkylaminocarbonyl, C_{4-9} cycloalkylaminocarbonyl, C_{8-17} aralkylaminocarbonyl, C_7 or C_{11} arylaminocarbonyl, C_{3-10} heterocyclylaminocarbonyl, C_{3-16} heteroaralkylaminocarbonyl, C_{2-7} alkylthiocarbonyl, C_{7-11} arylthiocarbonyl, C_{3-10} heteroarylthiocarbonyl, C_{2-7} alkoxythiocarbonyl, C_{4-9} cycloalkoxythiocarbonyl, C_{8-17} aralkoxythiocarbonyl, C_7 or C_{11} aryloxythiocarbonyl, aminothiocarbonyl, C_{2-7} alkylaminothiocarbonyl, C_{3-13} dialkylaminothiocarbonyl, C_{4-9} cycloalkylaminothiocarbonyl, C_{8-17} aralkylaminothiocarbonyl, C_7 or C_{11} arylaminothiocarbonyl, C_{3-10} heterocyclylaminothiocarbonyl, C_{3-16} heteroaralkylaminothiocarbonyl, or B is a natural or unnatural amino acid of L- or D-configuration substituted on the alpha-amine with H, C_{2-7} acyl, C_{7-11} aroyl, C_{3-10} heteroaroyl, C_{2-7} alkoxycarbonyl, C_{4-9} cycloalkoxycarbonyl, C_{8-17} aralkoxycarbonyl, C_7 or C_{11} aryloxycarbonyl, C_{2-10} heterocyclyloxycarbonyl, C_{3-15} heteroaralkoxycarbonyl, aminocarbonyl, C_{2-7} alkylaminocarbonyl, C_{3-13} dialkylaminocarbonyl, C_{4-9} cycloalkylaminocarbonyl, C_{8-17} aralkylaminocarbonyl, C_7 or C_{11} arylaminocarbonyl, C_{3-10} heterocyclylaminocarbonyl, C_{3-16} heteroaralkylaminocarbonyl, C_{2-7} alkylthiocarbonyl, C_{7-11} arylthiocarbonyl, C_{3-10} heteroarylthiocarbonyl, C_{2-7} alkoxythiocarbonyl, C_{4-9} cycloalkoxythiocarbonyl, C_{8-17} aralkoxythiocarbonyl, C_7 or C_{11} aryloxythiocarbonyl, aminothiocarbonyl, C_{2-7} alkylaminothiocarbonyl, C_{3-13} dialkylaminothiocarbonyl, C_{4-9} cycloalkylaminothiocarbonyl, C_{8-17} aralkylaminothiocarbonyl, C_7 or C_{11} arylaminothiocarbonyl, C_{3-10} heterocyclylaminothiocarbonyl, C_{3-16} heteroaralkylaminothiocarbonyl, C_{1-6} alkylsulfonyl, C_{3-8} cycloalkylsulfonyl, C_{7-16} aralkylsulfonyl, C_6 or C_{10} arylsulfonyl, C_{2-9} heterocyclylsulfonyl, or C_{2-15} heteroaralkylsulfonyl.

17. The compound of claim 16, wherein m is 1, R^0 is an optionally substituted 2-thiazole or 2-benzthiazole ring; R^2 is H or optionally substituted C_{1-6} alkyl, R^{17} is C_6 or C_{10} aryl, or C_{1-9} heteroaryl; and Y^1 is a bond and B is an optionally substituted C_{1-6} alkyl, C_{7-16} aralkyl, C_6 or C_{10} aryl, C_{1-9} heterocyclyl, or C_{2-15}

heterocyclylalkyl; or Y^1 is NH and B is C_{1-9} heterocyclyl or C_{2-15} heterocyclylalkyl.

18. The compound of claim 17, wherein m is 1, R^0 is 2-thiazole; R^2 is H; R^{17} is C_6 or C_{10} aryl, or C_{1-9} heteroaryl; Y^1 is NH and B is C_{1-9} heterocyclyl or C_{2-15} heterocyclylalkyl, and R^1 is 3-guanidinopropyl.

19. The compound of claim 16, wherein Y^1 is O or S.

20. The compound of claim 16, wherein

R^{17} is optionally substituted C_6 or C_{10} aryl, C_{1-9} heterocyclyl, C_{1-6} alkylthio, C_{3-8} cycloalkylthio, C_6 or C_{10} arylthio, C_{7-16} aralkylthio, C_{2-9} heterocyclylthio, or C_{2-15} heteroaralkylthio;

Y^1 is NH and B is C_{1-9} heterocyclyl or C_{2-15} heterocyclylalkyl.

21. The compound of claim 16, wherein

m is 1; W is N;Y^1 is NH; and R^{17} is an optionally substituted C_{3-8} cycloalkyl, C_6 or C_{10} aryl, or C_{1-9} heterocyclyl.

22. The compound of claim 1, wherein m is 0 and R^0 is H.

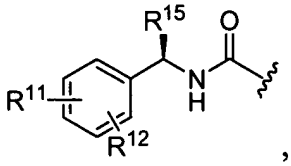
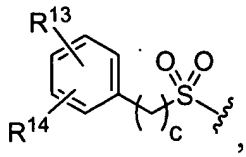
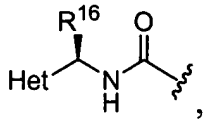
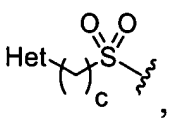
23. The compound of claim 22, wherein

R^2 is H or an optionally substituted C_{1-6} alkyl, C_{2-6} alkenyl, C_{3-8} cycloalkyl, C_{7-16} aralkyl, C_{8-16} aralkenyl, C_6 or C_{10} aryl, C_{2-9} heterocyclyl, C_{2-15} heteroaralkyl, or C_{3-15} heteroaralkenyl;

R^3 is H or C_{1-6} alkyl;

X is N; and

A is R^8-AA_2, wherein AA_2 is a single natural or unnatural alpha-amino acid residue and R^8 is selected from the group consisting of:


, 
, 
, and 
, wherein

c is 0 or 1;

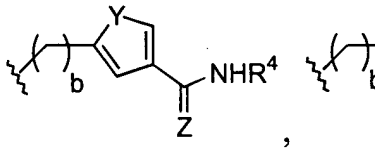
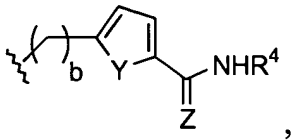
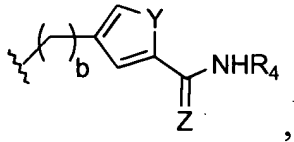
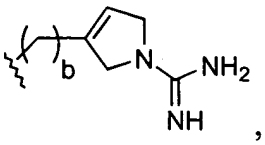
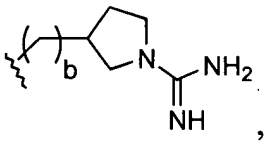
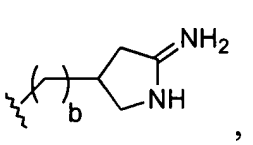
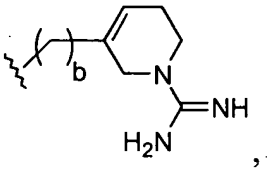
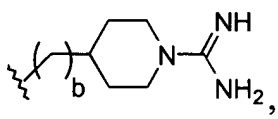
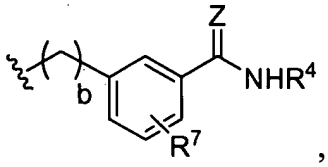
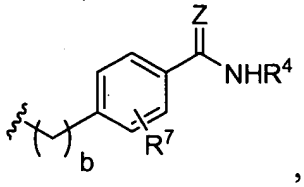
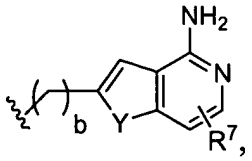
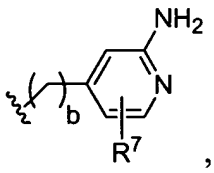
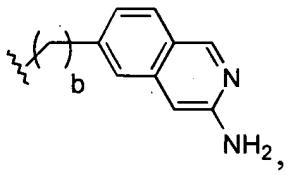
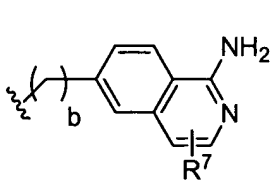
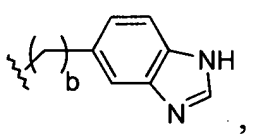
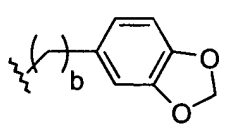
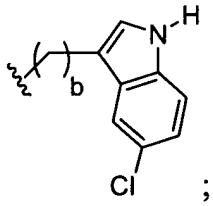
each of R^{11}, R^{12}, R^{13}, and R^{14} is, independently, C_{2-7} alkanoyl, C_{1-6} alkyl, C_{1-6} alkenyl, C_{1-6} alkoxy, C_{2-12} alkoxyalkyl, C_{1-6} alkylsulfinyl, C_{2-12} alkylsulfinylalkyl, C_{1-6} alkylsulfonyl, C_6 or C_{10} aryl, C_{7-16} arylalkyl, amino, C_{1-6} aminoalkyl, C_7 or C_{11} aryloyl, azido, C_{1-6} azidoalkyl, carboxaldehyde, carboxamide, carboxyl, C_{2-7} (carboxaldehyde)alkyl, C_{3-8} cycloalkyl, C_{4-14} cycloalkylalkyl, halo, C_{1-6} haloalkyl, C_{1-9} heterocyclyl, C_{1-9} (heterocyclyl)oxy, C_{2-10} (heterocyclyl)oyl, hydroxy, C_{1-6} hydroxyalkyl, nitro, C_{1-6} nitroalkyl, N-protected amino, N-protected aminoalkyl, C_{1-6} thioalkoxy, C_{2-12} thioalkoxyalkyl, C_{1-4} perfluoroalkyl, C_{1-4} perfluoroalkoxy, C_6 or C_{10} aryloxy, C_{3-8} cycloalkoxy, C_{4-14} cycloalkylalkoxy, or C_{7-16} arylalkoxy, -$(CH_2)_qCO_2R^A$, wherein q is zero to four and R^A is selected from the group consisting of (a) C_{1-6} alkyl, (b) C_6 or C_{10} aryl and (c) C_{7-16} arylalkyl, wherein the alkylene group is of one to six carbon atoms, -$(CH_2)_qCONR^BR^C$, wherein q is zero to four and R^B and R^C are independently selected from the group consisting of (a) hydrogen, (b) C_{1-6} alkyl, (c) C_6 or C_{10} aryl and (d) C_{7-16} arylalkyl, wherein the alkylene group is of one to six carbon atoms, -$(CH_2)_qSO_2R^D$, wherein q is zero to four and R^D is selected from the group consisting of (a) hydrogen, (b) C_{1-6} alkyl, (c) C_6 or C_{10} aryl and (d) C_{7-16} arylalkyl, wherein the alkylene group is of one to six carbon atoms, -$(CH_2)_qSO_2NR^ER^F$, wherein q is zero to four and R^E and R^F are independently selected from the group consisting of (a) hydrogen, (b) C_{1-6} alkyl, (c) C_6 or C_{10} aryl and (d) C_{7-16} arylalkyl, wherein the alkylene group is of one to six carbon atoms, or -$(CH_2)_qNR^GR^H$, wherein q is zero to four and R^G and R^H are independently selected from the group consisting of (a) hydrogen, (b) an N-protecting group, (c) alkyl of one to six carbon atoms, (d) alkenyl of two to six carbon atoms, (e) alkynyl of two to six carbon atoms, (f) C_6 or C_{10} aryl, (g) C_{7-16} arylalkyl, wherein the alkylene group is of one to six carbon atoms, (h) cycloalkyl

of three to eight carbon atoms, and (i) cycloalkylalkyl, wherein the cycloalkyl group is of three to eight carbon atoms, and the alkylene group is of one to ten carbon atoms, with the proviso that no two groups are bound to the nitrogen atom through a carbonyl group or a sulfonyl group; and

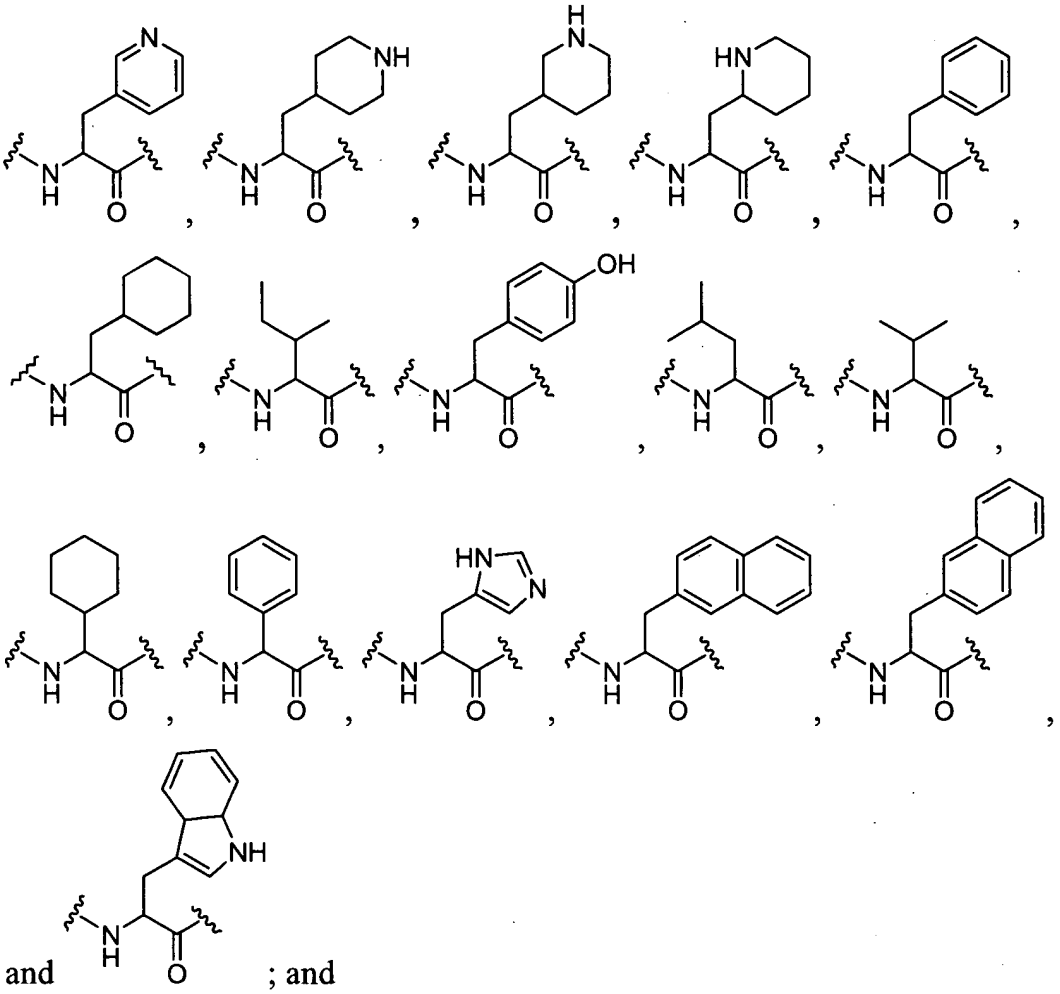
each of R^{15} and R^{16} is, independently, H, C_{1-6} alkyl; C_{1-6} hydroxyalkyl; C_{1-4} perfluoroalkyl, cyano, halo, $-(CH_2)_qCO_2R^A$, $-(CH_2)_qCONR^BR^C$, $-(CH_2)_qSO_2R^D$, $-(CH_2)_qSO_2NR^ER^F$, $-(CH_2)_qNR^GR^H$, wherein q is 0-2 and R^A, R^B, R^C, R^D, R^E, R^F, R^G, and R^H are as defined above.

24. The compound of claim 23, wherein

R^1 is selected from the group consisting of:

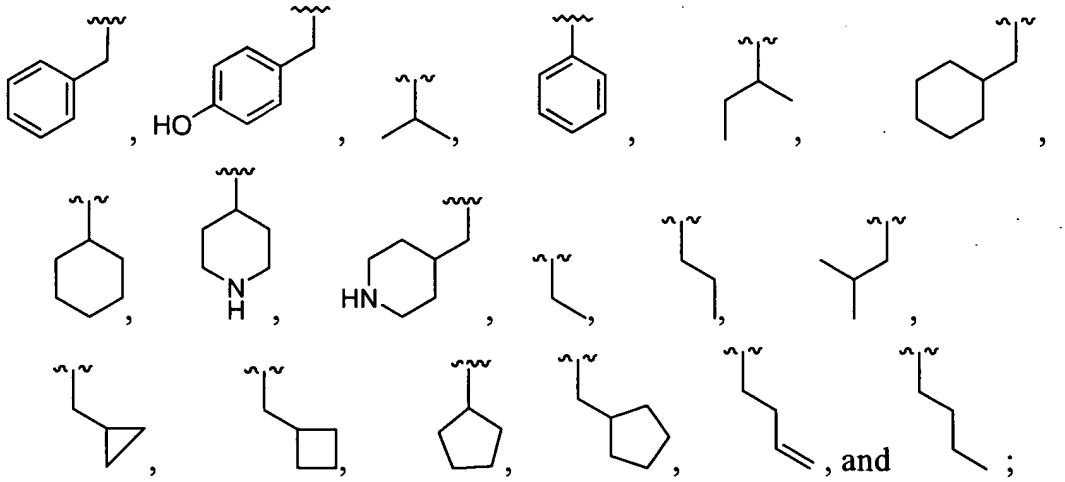

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

, and

;

AA_2 is selected from the group consisting of:



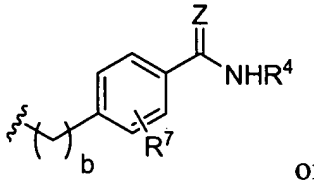
and ; and

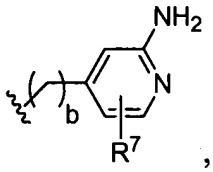
R^2 is selected from the group consisting of:



25. The compound of claim 24, wherein

R^1 is:



or


, wherein b is 0 or 1 and R^7 is H; and A is R^8-AA_2, wherein R^8 is benzylsulfonyl, 3-methylcarboxybenzylsulfonyl, 3-carboxybenzylsulfonyl, 2-nitrobenzylsulfonyl, 1-propylsulfonyl, and 3-chloropropylsulfonyl.

26. The compound of claim 1, wherein said compound further comprises a linker attached to any of the groups R^0, R^2, or A, wherein said linker is attached to a group reactive to a blood component.

27. The compound of claim 26, wherein said blood component is an erythrocyte, a lymphocyte, a blood platelet, an immunoglobulin, serum albumin, ferritin, corticosteroid-binding globulin, sex hormone-binding globulin, transferrin, thyroxin-binding protein, or alpha-2-macroglobulin.

28. The compound of claim 26, wherein said linker attached to a group reactive to a blood component is maleimide-$(CH_2)_{bb}C(O)NHCH_2CH_2(OCH_2CH_2)_{aa}OCH_2C(O)$-, maleimide-$(CH_2)_{bb}C(O)NHCH_2CH_2(OCH_2CH_2)_{aa}NHCH_2C(O)$-, maleimide-$(CH_2)_{bb}C(O)NHCH_2CH_2(OCH_2CH_2)_{aa}NHC(S)$-, maleimide-$(CH_2)_{bb}NHC(S)$-, maleimide-$(CH_2)_{bb}C(O)$-, or maleimide $(CH_2)_{bb}$-wherein aa is 1-10 and bb is 1-4.

29. The compound of claim 1, wherein said compound further comprises a polyethylene glycol moiety attached to any of the groups R^0, R^2, or A.

30. The compound of claim 29, wherein said said polyethylene glycol moiety is selected from the following group: $H(OCH_2CH_2)_{cc}O$-, $H_3C(OCH_2CH_2)_{cc}OC(O)$, $H(OCH_2CH_2)_{cc}OC(O)$, $H_3C(OCH_2CH_2)_{cc}NHC(O)$, $H(OCH_2CH_2)_{cc}NHC(O)$, $H_3C(OCH_2CH_2)_{cc}NHC(S)$, $H(OCH_2CH_2)_{cc}NHC(S)$, $H_3C(OCH_2CH_2)_{cc}C(O)$, $H(OCH_2CH_2)_{cc}C(O)$, $H_3C(OCH_2CH_2)_{cc}NHCH_2C(O)$, $H(OCH_2CH_2)_{cc}NHCH_2C(O)$, $H_3C(OCH_2CH_2)_{cc}OC(O)C(CH_3)_2$-, and $H(OCH_2CH_2)_{cc}OC(O)C(CH_3)_2$-, wherein cc is a range of numbers that results in an average molecular weight of said polyethylene glycol moiety of between 1,000-40,000.

31. The compound of claim 30, wherein cc is a range of numbers that results in an average molecular weight of said polyethylene glycol moiety of 20,000.

32. The compound of claim 30, wherein cc is a range of numbers that results in an average molecular weight of said polyethylene glycol moiety of 40,000.

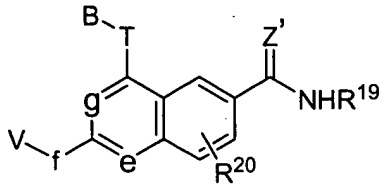
33. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of claim 1, or a pharmaceutically acceptable salt or prodrug thereof.

34. A method of treating a patient in need of thromboembolic disorder treatment comprising administering to said patient a therapeutically effective amount of a compound of claim 1, or a pharmaceutically acceptable salt or prodrug thereof.

35. The method of claim 34, wherein the thromboembolic disorder is selected from the group consisting of arterial cardiovascular thromboembolic disorders, venous cardiovascular thromboembolic disorders, and thromboembolic disorders in the chambers of the heart.

36. The method of claim 34, wherein the thromboembolic disorder is selected from unstable angina, an acute coronary syndrome, first myocardial infarction, recurrent myocardial infarction, ischemic sudden death, transient ischemic attack, stroke, atherosclerosis, peripheral occlusive arterial disease, venous thrombosis, deep vein thrombosis, thrombophlebitis, arterial embolism, coronary arterial thrombosis, cerebral arterial thrombosis, cerebral embolism, kidney embolism, pulmonary embolism, and thrombosis resulting from (a) prosthetic valves or other implants, (b) indwelling catheters, (c) stents, (d) cardiopulmonary bypass, (e) hemodialysis, or (f) other procedures in which blood is exposed to an artificial surface that promotes thrombosis.

37. A compound of formula II:



(II), or a pharmaceutically acceptable salt or prodrug thereof, wherein

R^{19} is H, C_{1-6} alkyl, or when taken together with R^{20} forms a fused 5- or 6-membered ring;

R^{20} is H, OH, SH, NH_2, NO_2, optionally substituted C_{1-6} alkyl, halogen, C_{1-3} perfluoroalkyl, or when together with Z' forms a fused 5- or 6-membered ring;

e is N, NO, or CR^{21a}, wherein R^{21a} is H, halogen, or C_{1-3} perfluoroalkyl;

g is N, NO, or CR^{21b}, wherein R^{21b} is H, halogen, C_{1-6} alkyl, C_{1-3} perfluoroalkyl, C_{1-3} alkenyl, C_{7-16} aralkyl, C_{2-15} heteroaralkyl, C_{1-6} alkoxy, C_{7-16} aralkoxy, C_{2-15} heteroaralkoxy, C_{2-7} alkoxycarbonyl, C_{8-17} aralkoxycarbonyl, C_{3-16} heteroaralkoxycarbonyl, C_{2-7} alkylaminocarbonyl, C_{8-17} aralkylaminocarbonyl, C_{3-16} heteroaralkylaminocarbonyl, C_{1-6} alkylthio, C_{7-16} aralkylthio, C_{2-15} heteroaralkylthio, C_{2-7} alkylthiocarbonyl, C_{8-17} aralkylthiocarbonyl, C_{3-16} heteroaralkylthiocarbonyl;

Z' is NR^{22}, (H, H), wherein R^{22} is H, C_{1-6} alkyl, OH, NH_2, NO_2, CO_2R^{22a}, wherein R^{22a} is C_{1-6} alkyl;

T is a bond, O, S, or NR^{23}, where R^{23} is H, OH, or optionally substituted C_{1-6} alkyl, C_{1-6} alkenyl, C_{7-11} aralkyl, C_{8-16} aralkenyl, C_{2-15} heteroaralkyl, or C_{3-15} heteroaralkenyl, wherein

when T is O, S, or NR^{23}, B is a natural or unnatural alpha-amino acid residue of D- or L-configuration, or an optionally substituted C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{1-6} alkenyl, C_{7-16} aralkyl, C_{8-17} aralkylcarbonyl, C_{8-16} aralkenyl, C_6 or C_{10} aryl, C_{2-15} heteroaralkyl, C_{3-16} heteroaralkylcarbonyl, C_{3-15} heteroaralkenyl, C_{2-7} acyl, C_{4-9} cycloalkylcarbonyl, C_{7-11} aroyl, C_{2-10} heterocyclyloyl, C_{4-9} cycloalkoxycarbonyl, C_7 or C_{11} aryloxycarbonyl, C_{3-10} heterocyclyloxycarbonyl, C_{3-16} heteroaralkyloxycarbonyl, aminocarbonyl, C_{2-7} alkylaminocarbonyl, C_{3-13} dialkylaminocarbonyl, C_{4-9} cycloalkylaminocarbonyl, C_{8-17} aralkylaminocarbonyl, C_7 or C_{11} arylaminocarbonyl, C_{3-10} heterocyclylaminocarbonyl, C_{3-16} heteroaralkylaminocarbonyl, C_{2-7} alkylthiocarbonyl, C_{4-9} cycloalkylthiocarbonyl, C_{7-11} arylthiocarbonyl, C_{8-17} aralkylthiocarbonyl, C_{2-10} heterocyclylthiocarbonyl, C_{3-16} heteroaralkylthiocarbonyl, aminothiocarbonyl, C_{2-7} alkylaminothiocarbonyl, C_{3-13} dialkylaminothiocarbonyl, C_{4-9} cycloalkylaminothiocarbonyl, C_{8-17} aralkylaminothiocarbonyl, C_7 or C_{11} arylaminothiocarbonyl, C_{3-10} heterocyclylaminothiocarbonyl, C_{3-16} heteroaralkylaminothiocarbonyl, C_{1-6} alkylsulfonyl, C_{3-8} cycloalkylsulfonyl, C_{7-16} aralkylsulfonyl, C_6 or C_{10} arylsulfonyl, C_{2-9} heterocyclylsulfonyl, or C_{2-15} heteroaralkylsulfonyl,

or when T is a bond, B is OH, SH, NH_2, NO_2, SO_3H, CO_2H or an optionally substituted C_{1-6} alkyl, C_{1-6} alkenyl, C_{7-16} aralkyl, C_{8-16} aralkenyl, C_{2-15} heteroaralkyl, C_{3-15} heteroaralkenyl, C_{2-7} acyl, C_{7-11} aroyl, C_{3-10} heteroaroyl, C_{2-7} alkoxycarbonyl, C_{4-9} cycloalkoxycarbonyl, C_{8-17} aralkoxycarbonyl, C_7 or C_{11} aryloxycarbonyl, C_{3-16} heteroaralkyloxycarbonyl, C_{2-10} heterocyclyloxycarbonyl, aminocarbonyl, C_{2-7} alkylaminocarbonyl, C_{3-13} dialkylaminocarbonyl, C_{4-9} cycloalkylaminocarbonyl, C_{8-17} aralkylaminocarbonyl, C_7 or C_{11} arylaminocarbonyl, C_{3-10}

heterocyclylaminocarbonyl, C_{3-16} heteroaralkylaminocarbonyl, C_{2-7} alkylthiocarbonyl, C_{4-9} cycloalkylthiocarbonyl, C_{7-11} arylthiocarbonyl, C_{8-17} aralkylthiocarbonyl, C_{2-10} heterocyclylthiocarbonyl, C_{3-16} heteroaralkylthiocarbonyl, C_{1-6} alkylsulfonyl, C_{3-8} cycloalkylsulfonyl, C_{7-16} aralkylsulfonyl, C_6 or C_{10} arylsulfonyl, C_{2-9} heterocyclylsulfonyl, or C_{2-15} heteroaralkylsulfonyl;

f is a bond, O, S, or NR^{24}, wherein R^{24} is H, OH, or C_{1-6} alkyl, wherein

when f is O, S, or NR^{24}, V is H or an optionally substituted C_{1-6} alkyl, C_{7-16} aralkyl, C_{2-15} heteroaralkyl, C_{2-7} acyl, C_{7-11} aroyl, C_{3-10} heteroaroyl, C_{2-7} alkoxycarbonyl, C_{4-9} cycloalkoxycarbonyl, C_{8-17} aralkoxycarbonyl, C_7 or C_{11} aryloxycarbonyl, C_{3-16} heteroaralkyloxycarbonyl, C_{2-10} heterocyclyloxycarbonyl, aminocarbonyl, C_{2-7} alkylaminocarbonyl, C_{3-13} dialkylaminocarbonyl, C_{4-9} cycloalkylaminocarbonyl, C_{8-17} aralkylaminocarbonyl, C_7 or C_{11} arylaminocarbonyl, C_{3-10} heterocyclylaminocarbonyl, C_{3-16} heteroaralkylaminocarbonyl, C_{2-7} alkylthiocarbonyl, C_{4-9} cycloalkylthiocarbonyl, C_{7-11} arylthiocarbonyl, C_{8-17} aralkylthiocarbonyl, C_{2-10} heterocyclylthiocarbonyl, C_{3-16} heteroaralkylthiocarbonyl, C_{1-6} alkylsulfonyl, C_{3-8} cycloalkylsulfonyl, C_{7-16} aralkylsulfonyl, C_6 or C_{10} arylsulfonyl, C_{2-9} heterocyclylsulfonyl, or C_{2-15} heteroaralkylsulfonyl,

or when f is a bond, V is H, OH, SH, NH_2, SO_3H, CO_2H, or an optionally substituted C_{1-6} alkyl, hydroxy-C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{1-6} alkenyl, C_{7-16} aralkyl, C_{8-16} aralkenyl, C_{2-15} heteroaralkyl, C_{3-15} heteroaralkyl, C_6 or C_{10} aryl, C_{1-9} heterocyclyl, C_{2-7} alkylaminocarbonyl, C_{3-13} dialkylaminocarbonyl, C_{4-9} cycloalkylaminocarbonyl, C_{8-17} aralkylaminocarbonyl, C_7 or C_{11} arylaminocarbonyl, C_{2-10} heterocyclylaminocarbonyl, C_{2-7} alkoxycarbonyl, C_{4-9} cycloalkoxycarbonyl, C_{8-17} aralkoxycarbonyl, C_7 or C_{11} aryloxycarbonyl, C_{3-10} heterocyclyloxycarbonyl, C_{3-16} heteroaralkyloxycarbonyl, C_{2-7} alkylthiocarbonyl, C_{4-9} cycloalkylthiocarbonyl, C_{7-11} arylthiocarbonyl, C_{8-17} aralkylthiocarbonyl, C_{2-10} heterocyclylthiocarbonyl, C_{3-16} heteroaralkylthiocarbonyl, C_{2-7} acyl, C_{7-11} aroyl, C_{3-}

$_{10}$ heteroaroyl, C_{1-6} alkylsulfonyl, C_{3-8} cycloalkylsulfonyl, C_{7-16} aralkylsulfonyl, C_6 or C_{10} arylsulfonyl, C_{2-9} heterocyclylsulfonyl, C_{2-15} heteroaralkylsulfonyl, C_{1-6} alkylaminosulfonyl, C_{3-8} cycloalkylaminosulfonyl, C_{2-12} dialkylaminosulfonyl, C_{7-17} aralkylaminosulfonyl, C_6 or C_{10} arylaminosulfonyl, C_{1-9} heterocyclylaminosulfonyl, C_{2-15} heteraralkylaminosulfonyl, C_{1-6} alkylsulfinyl, C_{3-8} cycloalkylsulfinyl, C_{7-16} aralkylsulfinyl, C_6 or C_{10} arylsulfinyl, C_{2-9} heterocyclylsulfinyl, or C_{2-15} heteroaralkylsulfinyl.

38. The compound of claim 37, wherein

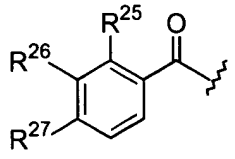
T is NR^{23}, wherein R^{23} is H;

B is an optionally substituted optionally substituted C_{2-7} acyl, C_{4-9} cycloalkylcarbonyl, C_{7-11} aroyl, C_{2-10} heterocyclylcarbonyl, C_{3-10} heteroaroyl, C_{2-7} alkoxycarbonyl, C_{4-9} cycloalkoxycarbonyl, C_{8-17} aralkoxycarbonyl, C_7 or C_{11} aryloxycarbonyl, C_{3-10} heterocyclyloxycarbonyl, C_{3-16} heteroaralkyloxycarbonyl, C_{2-7} alkylthiocarbonyl, C_{4-9} cycloalkylthiocarbonyl, C_{7-17} aralkylthiocarbonyl, C_7 or C_{11} arylthiocarbonyl, C_{3-16} heteroaralkylthiocarbonyl, C_{3-10} heterocyclylthiocarbonyl, aminothiocarbonyl, C_{2-7} alkylaminocarbonyl, C_{3-13} dialkylaminocarbonyl, C_{4-9} cycloalkylaminocarbonyl, C_{8-17} aralkylaminocarbonyl, C_7 or C_{11} arylaminocarbonyl, C_{3-10} heterocyclylaminocarbonyl, C_{3-16} heteroaralkylaminocarbonyl, C_{1-6} alkylsulfonyl, C_{3-8} cycloalkylsulfonyl, C_{7-16} aralkylsulfonyl, C_6 or C_{10} arylsulfonyl, C_{2-9} heterocyclylsulfonyl, or C_{2-15} heteroaralkylsulfonyl; and

f is O, S, or NR^{24}.

39. The compound of claim 37, wherein T is NR^{23}, wherein R^{23} is H, and B is an optionally substituted C_6 or C_{10} aroyl or an optionally substituted C_{1-9} heteroaroyl.

40. The compound of claim 39, wherein

B is  , wherein

each of R^{25}, R^{26},and R^{27} is, independently H, C_{2-7} alkanoyl, C_{1-6} alkyl, C_{1-6} alkenyl, C_{1-6} alkoxy, C_{2-12} alkoxyalkyl, C_{1-6} alkylsulfinyl, C_{2-12} alkylsulfinylalkyl, C_{1-6} alkylsulfonyl, C_6 or C_{10} aryl, C_{7-16} arylalkyl, amino, C_{1-6} aminoalkyl, C_7 or C_{11} aryloyl, azido, C_{1-6} azidoalkyl, carboxaldehyde, carboxamide, carboxyl, C_{2-7} (carboxaldehyde)alkyl, C_{3-8} cycloalkyl, C_{4-14} cycloalkylalkyl, halo, C_{1-6} haloalkyl, C_{1-9} heterocyclyl, C_{1-9} (heterocyclyl)oxy, C_{2-10} (heterocyclyl)oyl, hydroxy, C_{1-6} hydroxyalkyl, nitro, cyano, C_{1-6} nitroalkyl, N-protected amino, N-protected aminoalkyl, C_{1-6} thioalkoxy, C_{2-12} thioalkoxyalkyl, thiol, $-(CH_2)_qCO_2R^A$, wherein q is zero to four and R^A is selected from the group consisting of (a) C_{1-6} alkyl, (b) C_6 or C_{10} aryl and (c) C_{7-16} arylalkyl, wherein the alkylene group is of one to six carbon atoms, $-(CH_2)_qCONR^BR^C$, wherein q is zero to four and R^B and R^C are independently selected from the group consisting of (a) hydrogen, (b) C_{1-6} alkyl, (c) C_6 or C_{10} aryl and (d) C_{7-16} arylalkyl, wherein the alkylene group is of one to six carbon atoms, $-(CH_2)_qSO_2R^D$, wherein q is zero to four and R^D is selected from the group consisting of (a) hydrogen, (b) C_{1-6} alkyl, (c) C_6 or C_{10} aryl and (d) C_{7-16} arylalkyl, wherein the alkylene group is of one to six carbon atoms, $-(CH_2)_qSO_2NR^ER^F$, wherein q is zero to four and R^E and R^F are independently selected from the group consisting of (a) hydrogen, (b) C_{1-6} alkyl, (c) C_6 or C_{10} aryl and (d) C_{7-16} arylalkyl, wherein the alkylene group is of one to six carbon atoms, $-(CH_2)_qNR^GR^H$, wherein q is zero to four and R^G and R^H are independently selected from the group consisting of (a) hydrogen, (b) an N-protecting group, (c) alkyl of one to six carbon atoms, (d) alkenyl of two to six carbon atoms, (e) alkynyl of two to six carbon atoms, (f) C_6 or C_{10} aryl, (g) C_{7-16} arylalkyl, wherein the alkylene group is of one to six carbon atoms, (h) cycloalkyl of three to eight carbon atoms, and (i) cycloalkylalkyl, wherein the cycloalkyl group is of three to eight carbon atoms, and the alkylene group is of one to ten carbon atoms, with the proviso that

no two groups are bound to the nitrogen atom through a carbonyl group or a sulfonyl group, C_{1-4} perfluoroalkyl, C_{1-4} perfluoroalkoxy; C_6 or C_{10} aryloxy, C_{3-8} cycloalkoxy, C_{4-14} cycloalkylalkoxy, or C_{7-16} arylalkoxy.

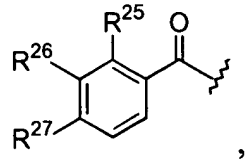
41. The compound of claim 40, wherein f is a bond and V is an optionally substituted C_{1-6} alkyl, hydroxy-C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{1-6} alkenyl, C_{7-16} aralkyl, C_{8-16} aralkenyl, C_{2-15} heteroaralkyl, C_{3-15} heteroaralkyl, C_6 or C_{10} aryl, C_{1-9} heterocyclyl, C_{2-7} alkylaminocarbonyl, C_{3-13} dialkylaminocarbonyl, C_{4-9} cycloalkylaminocarbonyl, C_{8-17} aralkylaminocarbonyl, C_7 or C_{11} arylaminocarbonyl, C_{2-10} heterocyclylaminocarbonyl, C_{2-7} alkoxycarbonyl, C_{4-9} cycloalkoxycarbonyl, C_{8-17} aralkoxycarbonyl, C_7 or C_{11} aryloxycarbonyl, C_{3-10} heterocyclyloxycarbonyl, C_{3-16} heteroaralkyloxycarbonyl, C_{2-7} alkylthiocarbonyl, C_{4-9} cycloalkylthiocarbonyl, C_{7-11} arylthiocarbonyl, C_{8-17} aralkylthiocarbonyl, C_{2-10} heterocyclylthiocarbonyl, C_{3-16} heteroaralkylthiocarbonyl, C_{2-7} acyl, C_{7-11} aroyl, C_{3-10} heteroaroyl, C_{1-6} alkylsulfonyl, C_{3-8} cycloalkylsulfonyl, C_{7-16} aralkylsulfonyl, C_6 or C_{10} arylsulfonyl, C_{2-9} heterocyclylsulfonyl, or C_{2-15} heteroaralkylsulfonyl, C_{1-6} alkylaminosulfonyl, C_{3-8} cycloalkylaminosulfonyl, C_{2-12} dialkylaminosulfonyl, C_{7-17} aralkylaminosulfonyl, C_6 or C_{10} arylaminosulfonyl, C_{1-9} heterocyclylaminosulfonyl, C_{2-15} heteraralkylaminosulfonyl, C_{1-6} alkylsulfinyl, C_{3-8} cycloalkylsulfinyl, C_{7-16} aralkylsulfinyl, C_6 or C_{10} arylsulfinyl, C_{2-9} heterocyclylsulfinyl, or C_{2-15} heteroaralkylsulfinyl.

42. The compound of claim 41, wherein f is a bond and V is optionally substituted C_6 or C_{10} arylaminocarbonyl or C_{7-17} aralkylaminocarbonyl.

43. The compound of claim 41, wherein R^{25} is H, halo, or C_{1-6} alkyl; R^{26} is OH; and R^{27} is H.

44. The compound of claim 37, wherein f is a bond and V is H.

45. The compound of claim 44, wherein

B is  , wherein

each of R^{25}, R^{26},and R^{27} is, independently H, C_{2-7} alkanoyl, C_{1-6} alkyl, C_{1-6} alkenyl, C_{1-6} alkoxy, C_{2-12} alkoxyalkyl, C_{1-6} alkylsulfinyl, C_{2-12} alkylsulfinylalkyl, C_{1-6} alkylsulfonyl, C_6 or C_{10} aryl, C_{7-16} arylalkyl, amino, C_{1-6} aminoalkyl, C_7 or C_{11} aryloyl, azido, C_{1-6} azidoalkyl, carboxaldehyde, carboxamide, carboxyl, C_{2-7} (carboxaldehyde)alkyl, C_{3-8} cycloalkyl, C_{4-14} cycloalkylalkyl, halo, C_{1-6} haloalkyl, C_{1-9} heterocyclyl, C_{1-9} (heterocyclyl)oxy, C_{2-10} (heterocyclyl)oyl, hydroxy, C_{1-6} hydroxyalkyl, nitro, C_{1-6} nitroalkyl, N-protected amino, N-protected aminoalkyl, C_{1-6} thioalkoxy, C_{2-12} thioalkoxyalkyl, thiol, $-(CH_2)_qCO_2R^A$, wherein q is zero to four and R^A is selected from the group consisting of (a) C_{1-6} alkyl, (b) C_6 or C_{10} aryl and (c) C_{7-16} arylalkyl, wherein the alkylene group is of one to six carbon atoms, $-(CH_2)_qCONR^BR^C$, wherein q is zero to four and R^B and R^C are independently selected from the group consisting of (a) hydrogen, (b) C_{1-6} alkyl, (c) C_6 or C_{10} aryl and (d) C_{7-16} arylalkyl, wherein the alkylene group is of one to six carbon atoms, $-(CH_2)_qSO_2R^D$, wherein q is zero to four and R^D is selected from the group consisting of (a) hydrogen, (b) C_{1-6} alkyl, (c) C_6 or C_{10} aryl and (d) C_{7-16} arylalkyl, wherein the alkylene group is of one to six carbon atoms, $-(CH_2)_qSO_2NR^ER^F$, wherein q is zero to four and R^E and R^F are independently selected from the group consisting of (a) hydrogen, (b) C_{1-6} alkyl, (c) C_6 or C_{10} aryl and (d) C_{7-16} arylalkyl, wherein the alkylene group is of one to six carbon atoms, $-(CH_2)_qNR^GR^H$, wherein q is zero to four and R^G and R^H are independently selected from the group consisting of (a) hydrogen, (b) an N-protecting group, (c) alkyl of one to six carbon atoms, (d) alkenyl of two to six carbon atoms, (e) alkynyl of two to six carbon atoms, (f) C_6 or C_{10} aryl, (g) C_{7-16} arylalkyl, wherein the alkylene group is of one to six carbon atoms, (h) cycloalkyl of three to eight carbon atoms,

and (i) cycloalkylalkyl, wherein the cycloalkyl group is of three to eight carbon atoms, and the alkylene group is of one to ten carbon atoms, with the proviso that no two groups are bound to the nitrogen atom through a carbonyl group or a sulfonyl group, C_{1-4} perfluoroalkyl, C_{1-4} perfluoroalkoxy; C_6 or C_{10} aryloxy, C_{3-8} cycloalkoxy, C_{4-14} cycloalkylalkoxy, or C_{7-16} arylalkoxy.

46. The compound of claim 45, wherein R^{25} is H, halo, or C_{1-6} alkyl; R^{26} is OH; and R^{27} is H.

47. The compound of claim 37, wherein said compound further comprises a linker attached to any of the groups B or V, wherein said linker is attached to a group reactive to a blood component.

48. The compound of claim 47, wherein said blood component is an erythrocyte, a lymphocyte, a blood platelet, an immunoglobulin, serum albumin, ferritin, corticosteroid-binding globulin, sex hormone-binding globulin, transferrin, thyroxin-binding protein, or alpha-2-macroglobulin.

49. The compound of claim 47, wherein said linker attached to a group reactive to a blood component is maleimide-$(CH_2)_{bb}C(O)NHCH_2CH_2(OCH_2CH_2)_{aa}OCH_2C(O)$-, maleimide-$(CH_2)_{bb}C(O)NHCH_2CH_2(OCH_2CH_2)_{aa}NHCH_2C(O)$-, maleimide-$(CH_2)_{bb}C(O)NHCH_2CH_2(OCH_2CH_2)_{aa}NHC(S)$-, maleimide-$(CH_2)_{bb}NHC(S)$, maleimide-$(CH_2)_{bb}C(O)$-, or maleimide-$(CH_2)_{bb}$-, wherein aa is 1-10 and bb is 1-4.

50. The compound of claim 37, wherein said compound further comprises a polyethylene glycol moiety attached to any of the groups B or V.

51. The compound of claim 50, wherein said said polyethylene glycol moiety is selected from the following group: $H(OCH_2CH_2)_{cc}O$-, $H_3C(OCH_2CH_2)_{cc}OC(O)$, $H(OCH_2CH_2)_{cc}OC(O)$, $H_3C(OCH_2CH_2)_{cc}NHC(O)$, $H(OCH_2CH_2)_{cc}NHC(O)$, $H_3C(OCH_2CH_2)_{cc}NHC(S)$, $H(OCH_2CH_2)_{cc}NHC(S)$, $H_3C(OCH_2CH_2)_{cc}C(O)$, $H(OCH_2CH_2)_{cc}C(O)$, $H_3C(OCH_2CH_2)_{cc}NHCH_2C(O)$, $H(OCH_2CH_2)_{cc}NHCH_2C(O)$, $H_3C(OCH_2CH_2)_{cc}OC(O)C(CH_3)_2$-, and $H(OCH_2CH_2)_{cc}OC(O)C(CH_3)_2$-, wherein cc is a range of numbers that results in an average molecular weight of said polyethylene glycol moiety of between 1,000-40,000.

52. The compound of claim 50, wherein cc is a range of numbers that results in an average molecular weight of said polyethylene glycol moiety of 20,000.

53. The compound of claim 51, wherein cc is a range of numbers that results in an average molecular weight of said polyethylene glycol moiety of 40,000.

54. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of claim 37, or a pharmaceutically acceptable salt or prodrug thereof.

55. A method of treating a patient in need of thromboembolic disorder treatment comprising administering to said patient a therapeutically effective amount of a compound of claim 37, or a pharmaceutically acceptable salt or prodrug thereof.

56. The method of claim 55, wherein the thromboembolic disorder is selected from the group consisting of arterial cardiovascular thromboembolic disorders, venous cardiovascular thromboembolic disorders, and thromboembolic disorders in the chambers of the heart.

57. The method of claim 55, wherein the thromboembolic disorder is selected from unstable angina, an acute coronary syndrome, first myocardial infarction, recurrent myocardial infarction, ischemic sudden death, transient ischemic attack, stroke, atherosclerosis, peripheral occlusive arterial disease, venous thrombosis, deep vein thrombosis, thrombophlebitis, arterial embolism, coronary arterial thrombosis, cerebral arterial thrombosis, cerebral embolism, kidney embolism, pulmonary embolism, and thrombosis resulting from (a) prosthetic valves or other implants, (b) indwelling catheters, (c) stents, (d) cardiopulmonary bypass, (e) hemodialysis, or (f) other procedures in which blood is exposed to an artificial surface that promotes thrombosis.

58. A computer comprising a processor in electrical communication with a memory; said memory having stored therein

(i) atomic coordinates, or surrogates thereof, in one or more of the files listed in Figure 16 for all of the non-hydrogen atoms of residues serine 195, histidine 57, and aspartic acid 102 of Factor XI catalytic domain or atomic coordinates that have a root mean square deviation from the backbone atoms of said residues of less than 0.4 Å; and

(ii) a program for displaying a three-dimensional model of said Factor XI catalytic domain.

59. A computer comprising a processor in electrical communication with a memory; said memory having stored therein

(i) x-ray diffraction data for all of the non-hydrogen atoms of residues serine 195, histidine 57, and aspartic acid 102 of Factor XI catalytic domain or x-ray diffraction data for amino acids that have a root mean square deviation from the backbone atoms of said residues of less than 0.4 Å; and

(ii) a program for displaying a three-dimensional model of said Factor XI catalytic domain.

60. A computer comprising a processor in electrical communication with a memory; said memory having stored therein a pharmacophore model of Factor XI ligands and a program for displaying said model, said model comprising at least three of the following:

(i) an electrophilic carbon atom that binds to the side chain oxygen atom (OG) of Ser195 such that the electrophilic carbon atom is 1.4 to 4.0 Å from said oxygen atom;

(ii) at least one hydrogen bond donor group to interact with Asp189 such that the non-hydrogen atoms of the hydrogen bond donor groups are 2.0 to 4.2 Å away from the side chain oxygens of Asp189;

(iii) a hydrophobic group that makes one or more van der Waals contacts with residues of the active site and is less than 5.0 Å away from the CB atom of Ala97;

(iv) a hydrogen bond donor group which makes a hydrogen bond with the main chain carbonyl of Ser214 such that the distance between the hydrogen-bonded atoms is less than 4.0 Å;

(v) a hydrogen bond donor group that makes a hydrogen bond with the main chain carbonyl of Gly216 such that the distance between the hydrogen-bonded atoms is less than 4.0 Å;

(vi) a hydrogen bond acceptor group that makes a hydrogen bond with the main chain nitrogen of Gly216 such that the distance between the hydrogen-bonded atoms is less than 4.0 Å;

(vii) a hydrogen bond acceptor group that makes a hydrogen bond with a side chain nitrogen of His57 such that the distance between the hydrogen-bonded atoms is less than 4.0 Å;

(viii) a group that makes one or more van der Waals contacts with the side chains of residues of Lys192 and/or Leu146;

(ix) a group that makes one or more van der Waals contacts with the side chains of residues of Cys191 and/or Cys219; and

(x) a group or groups that make participate in one or more polar interactions with the side chain of residue of His174, Glu98, and/or Glu217.

61. A method of selecting or designing a candidate ligand for Factor XIa, said method comprising the steps of:

(a) generating in a computer a three-dimensional structure of Factor XI catalytic domain based on the atomic coordinates in one or more of the files listed in Figure 16 for all of the non-hydrogen atoms of residues serine 195, histidine 57, and aspartic acid 102 or atomic coordinates that have a root mean square deviation from the backbone atoms of said residues of less than 0.4 Å; and

(b) selecting or designing a candidate ligand having sufficient surface complementary to said structure to bind Factor XIa in an aqueous solution.

62. The method of claim 61, further comprising determining the ability of said candidate ligand to bind said Factor XIa *in vitro* or *in vivo*.

63. The method of claim 61, further comprising determining the ability of said candidate ligand to inhibit the enzymatic activity of said Factor XIa *in vitro* or *in vivo*.

64. The method of claim 61, wherein said three-dimensional structure further comprises the hydrogen atoms of residues serine 195, histidine 57, and aspartic acid 102.

65. The method of claim 64, wherein said three-dimensional structure further comprises the non-hydrogen atoms of residues Tyr5901, Ala97, Glu98, ASP 102,

Ile146, His174, Asp189, Ala190, Cys191, Lys192, Gly193, Asp194, Ser214, Trp215, Gly216, Glu217, and Gly218.

66. The method of claim 65, wherein said three-dimensional structure further comprises the hydrogen atoms of residues Tyr5901, Ala97, Glu98, ASP 102, Ile146, His174, Asp189, Ala190, Cys191, Lys192, Gly193, Asp194, Ser214, Trp215, Gly216, Glu217, and Gly218.

67. A method for manufacturing a Factor XIa ligand, said method comprising the steps of:

(a) obtaining the atomic coordinates of at least a portion of Factor XI catalytic domain with a ligand;

(b) selecting one or more moieties in said ligand to be modified; wherein said modified ligand maintains the ability to bind said Factor XI; and

(c) modifying said ligand based on said determination.

68. The method of claim 67, further comprising determining the ability of said candidate ligand to bind said Factor XIa *in vitro* or *in vivo*.

69. The method of claim 67, further comprising determining the ability of said candidate ligand to inhibit the enzymatic activity of said Factor XIa *in vitro* or *in vivo*.

70. The method of claim 67, wherein said atomic coordinates further comprises the hydrogen atoms of residues serine 195, histidine 57, and aspartic acid 102.

71. The method of claim 70, wherein said atomic coordinates further comprises the non-hydrogen atoms of residues Tyr5901, Ala97, Glu98, ASP 102, Ile146,

His174, Asp189, Ala190, Cys191, Lys192, Gly193, Asp194, Ser214, Trp215, Gly216, Glu217, and Gly218.

72. The method of claim 71, wherein said atomic coordinates further comprises the hydrogen atoms of residues Tyr5901, Ala97, Glu98, ASP 102, Ile146, His174, Asp189, Ala190, Cys191, Lys192, Gly193, Asp194, Ser214, Trp215, Gly216, Glu217, and Gly218.

73. The method of claim 67, further comprising crystallizing Factor XI catalytic domain (FXIcat) with a ligand.

74. The method of claim 67, wherein said ligand specifically binds said FXIcat.

75. The method of claim 67, wherein said modification increases the affinity of said ligand for said FXIcat.

76. The method of claim 67, wherein said modification increases the aqueous solubility of said ligand.

77. The method of claim 67, wherein said modification increases the blood circulation half-life of said ligand *in vivo*.

78. A method for manufacturing a Factor XI catalytic domain ligand, said method comprising manufacturing a ligand that binds Factor XIa; wherein said ligand is designed or selected based on information obtained using a model of the atomic coordinates of at least a portion of said Factor XI catalytic domain.

79. A method of evaluating the ability of a candidate ligand to bind Factor XIa, the method comprising the steps of:

(a) generating in a computer a three-dimensional structure of Factor XI catalytic domain based on the atomic coordinates in one or more of the files listed in Figure 16 of all of the non-hydrogen atoms of residues serine 195, histidine 57, and aspartic acid 102 or atomic coordinates that have a root mean square deviation from the backbone atoms of said residues of less than 0.4 Å; and

(b) employing computational means to measure the interaction between said candidate ligand and said Factor XI catalytic domain.

80. The method of claim 79, further comprising determining the ability of said candidate ligand to bind said Factor XIa *in vitro* or *in vivo*.

81. The method of claim 79, further comprising determining the ability of said candidate ligand to inhibit the enzymatic activity of said Factor XIa *in vitro* or *in vivo*.

82. The method of claim 79, wherein said three-dimensional structure further comprises the hydrogen atoms of residues serine 195, histidine 57, and aspartic acid 102.

83. The method of claim 82, wherein said three-dimensional structure further comprises the non-hydrogen atoms of residues Tyr5901, Ala97, Glu98, ASP 102, Ile146, His174, Asp189, Ala190, Cys191, Lys192, Gly193, Asp194, Ser214, Trp215, Gly216, Glu217, and Gly218.

84. The method of claim 83, wherein said three-dimensional structure further comprises the hydrogen atoms of residues Tyr5901, Ala97, Glu98, ASP 102, Ile146, His174, Asp189, Ala190, Cys191, Lys192, Gly193, Asp194, Ser214, Trp215, Gly216, Glu217, and Gly218.

85. A method of identifying a candidate ligand for Factor XIa, the method comprising the steps of:

(a) generating a three-dimensional pharmacophore model of Factor XI catalytic domain ligands using a computer of claim 60; and

(b) selecting a candidate ligand satisfying the criteria of said pharmacophore model.

86. The method of claim 85, further comprising determining the ability of said candidate ligand to bind said Factor XIa *in vitro* or *in vivo*.

87. The method of claim 85, further comprising determining the ability of said candidate ligand to inhibit the enzymatic activity of said Factor XIa *in vitro* or *in vivo*.

88. The method of claim 85, wherein said three-dimensional pharmacophore model further comprises the hydrogen atoms of residues serine 195, histidine 57, and aspartic acid 102.

89. The method of claim 88, wherein said three-dimensional pharmacophore model further comprises the non-hydrogen atoms of residues Tyr5901, Ala97, Glu98, ASP 102, Ile146, His174, Asp189, Ala190, Cys191, Lys192, Gly193, Asp194, Ser214, Trp215, Gly216, Glu217, and Gly218.

90. The method of claim 89, wherein said three-dimensional pharmacophore model further comprises the hydrogen atoms of residues Tyr5901, Ala97, Glu98, ASP 102, Ile146, His174, Asp189, Ala190, Cys191, Lys192, Gly193, Asp194, Ser214, Trp215, Gly216, Glu217, and Gly218.

91. A crystal of Factor XI that has a size of at least 10 μ in the smallest dimension.

92. A method of obtaining a structural model of a Factor XI catalytic domain of interest, said method comprising homology modeling using at least a portion of the atomic coordinates in one or more of the files listed in Figure 16 and at least a portion of the amino acid sequence of said Factor XI catalytic domain of interest, thereby generating a model of said Factor XI catalytic domain of interest.

93. A method of determining the three-dimensional structure of a Factor XI of interest, said method comprising the steps of:

(a) crystallizing said Factor XI catalytic domain of interest;

(b) generating an X-ray diffraction pattern from said crystallized Factor XI catalytic domain of interest; and

(c) applying at least a portion of the atomic coordinates in one or more of the files listed in Figure 16 to said diffraction pattern to generate a three-dimensional electron density map of at least a portion of said Factor XI catalytic domain of interest.

94. A purified, less than full-length fragment of Factor XI comprising residues 370-607 of SEQ ID NO: 1 (human Factor XIa).

95. A nucleic acid encoding a protein of claim 94.

96. A purified, less than full-length fragment of Factor XI comprising residues 369-606 of SEQ ID NO: 2 (rabbit Factor XIa).

97. A nucleic acid encoding a protein of claim 96.

98. A purified, less than full-length fragment of Factor XI comprising residues 372-606 of SEQ ID NO: 3 (mouse Factor XIa) or residues 1-234 of SEQ ID NO: 4 (rat Factor XIa).

99. A nucleic acid encoding a protein of claim 98.

100. A purified Factor XI protein or fragment thereof comprising a mutation, wherein said mutation is

(a) a mutation that enhances the ability of Factor XI catalytic domain to crystallize,

(b) a mutation of a residue that is otherwise post-translationally modified in an organism used for recombinant expression,

(c) a mutation that alters the charge of Factor XI,

(d) a mutation that eliminates a free, reactive sulfhydryl group of a cysteine,

(e) a combination of mutations that together alter the distribution of charge density without altering the overall charge of Factor XI,

(f) a mutation of the NH_2- or COOH-terminal residue of Factor XI, or

(g) a mutation that alters the folding of Factor XI.

101. A nucleic acid encoding a protein of claim 100.

102. The protein or fragment of claim 100 comprising one of the following mutations:

(i) S434A;

(ii) T475A;

(iii) S434A, T475A;

(iv) S434A, T475A, K422A

(v) S434A, T475A, K437A;

(vi) S434A, T475A, K486A;

(vii) S434A, T475A, K505A;

(viii) S434A, T475A, K509A;

(ix) S434A, T475A, C482S;

(x) S434A, T475A, C482S, K437A;

(xi) S434A, T475A, C482S, R479A;

(xii) S434A, T475A, C482S, K505A;

(xiii) S434A, T475A, C482S, D476A;

(xiv) S434A, T475A, AVC-terminal trucation; or

(xv) S434A, T475A, C482S, Y416S.

103. A nucleic acid encoding a protein of claim 102.